UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: 7 June 2016

SUBJECT: Furfural. Human-Health Risk Assessment for Proposed Use on Bare Soil; Revised Assessment for Golf Course Turf, Athletic Fields, Sod Farms and Outdoor Ornamentals.

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Decision No.: 467035
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40 CFR:

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration Division (RD) of OPP has requested that HED conduct occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from the proposed use of furfural on bare soil. In addition, a revised human-health risk assessment was conducted for registered uses on golf course turf (greens, tees, and spot treatment of fairways/roughs), athletic fields, sod farms and outdoor ornamentals, based on the cancer reclassification of furfural and furfuryl alcohol.

Table of Contents

INTRODUCTION

A summary of the findings and an assessment of human-health risk resulting from the proposed use of furfural are provided in this document. The HED team members contributing to this risk assessment include: Thurston Morton (dietary exposure assessment), Jessica Kidwell (toxicology assessment) and Kelly O'Rourke (occupational and residential exposure assessment and overall risk assessment). The Environmental Fate and Effects Division (EFED) team members include: Gabe Rothman and José Meléndez (review of volatility and fate data, flux estimates and drinking water assessment).

1. EXECUTIVE SUMMARY

The Health Effects Division (HED) has conducted a human-health risk assessment for the active ingredient furfural for the proposed use on bare soil. In addition, a revised human-health risk assessment has been conducted for previously registered uses on golf course turf (tees, greens and spot treatment of fairways/roughs), athletic fields, sod farms and outdoor ornamentals, based on the cancer reclassification of furfural and furfuryl alcohol (a soil degradate of furfural). It is also currently registered for use in greenhouses, though it is not marketed for this use. Furfural has a vapor pressure of 2.6 mm Hg, considered quite volatile relative to typical insecticides/fungicides, and is proposed for use rates up to 69.5 pounds active ingredient per acre (lb ai/A). Therefore, the inhalation route is expected to be a significant component of overall exposure, and has been emphasized in this assessment.

*Proposed/Re-evaluated Use*s

In this action, the end-use product containing 90% furfural in an emulsifiable concentrate formulation (MULTIGUARD PROTECT® EC, EPA Reg. No. 75753-1, proposed label dated 2/17/2016) is proposed for use on bare soil as a pre-plant treatment for fruiting vegetables, cucurbits, citrus, pome fruit, stone fruit, berries and tree nuts. A one-time application is proposed at pre-plant, at a rate of 69.5 lb ai/A via chemigation under tarps, or shank injection/rotovation followed immediately by tarping.

For the currently registered uses that are being reassessed, the label indicates application rates ranging from 47.7 lb ai/A to 69.5 lb ai/A, up to 6 times per season, at 14- to 28-day intervals for athletic fields, golf courses and sod farms. The only application equipment/method permitted for these uses on the proposed label is groundboom sprayer. For outdoor ornamentals, post-plant application rates range from 19.5 lb ai/A to 47.7 lb ai/A, up to 8 times per crop, at 14- to 28-day intervals, by chemigation only (drip tubes/tapes). Drench application rates range from 0.174 lb ai/100 gal to 0.339 lb ai/100 gal, at 7- to 28-day intervals via a mechanically-pressurized handgun sprayer.

Note: In a letter dated February 9, 2016, the registrant requested that this proposed action be considered as a time-limited registration with a "sunset" of 5 years to allow time for cancer mode of action data to be generated. Therefore, in addition to estimating cancer risks using the standard assumptions for exposure duration (i.e. 35 years for occupational handlers and 50 years for bystander), cancer risks were also estimated based on the time-limited durations of 5 years

for the proposed new use, and 10 years for the existing uses (which have already been registered for 5 years and will continue for another 5 under the time-limited registration).

Exposure Profile

The proposed (bare soil) and currently-registered use patterns (golf courses, sod farms, athletic fields, and ornamentals) are considered non-food uses. However, because of the high application rate of furfural, and the large amounts of water used during and after application, furfural may inadvertently be transported into drinking water sources. Therefore, to be health protective, the HED evaluated the potential dietary exposure associated with drinking water. Furfural has a vapor pressure of 2.6 mm Hg and is considered volatile relative to typical insecticides/fungicides. Therefore, the inhalation route is expected to be a significant component of overall exposure. For the general public, inhalation exposure is expected to be the major route of exposure. Occupational workers have potential for both inhalation and dermal exposure.

Currently registered uses of furfural are considered non-food and are, therefore, not subject to the 1996 Food Quality Protection Act (FQPA). However, it is EPA's policy to apply risk assessment techniques developed in the implementation of the FQPA to any pesticide risk assessment, whether it falls under the FQPA or not, so long as application of the risk assessment technique is consistent with good scientific practice and is not otherwise prohibited by law.

Hazard Characterization

The hazard database for furfural is complete. Several inhalation studies are available and include a special acute portal-of-entry study as well as repeat dosing inhalation studies. Respiratory effects, both at the portal of entry (the nose) and in the deep lung (pulmonary effects) were observed across the inhalation studies. The portal-of-entry effects (e.g. nasal inflammation as indicated by infiltration of inflammatory cells, hyperplasia, and degeneration) occur at lower concentrations than the pulmonary effects (breathing abnormalities that can progress to mortality at high doses), and so protecting for portal-of-entry effects protects for pulmonary effects. Importantly, portal-of-entry effects of low severity (e.g., slight nasal inflammation) that occur after a single exposure are completely reversible within two weeks.

Exposure to furfural via the oral and dermal routes also results in pulmonary toxicity indicative of respiratory distress, which likely mediates the mortality observed at high dose levels of furfural. For the oral route only, liver toxicity is also observed, but at lower doses than those that cause pulmonary toxicity, and so protecting for liver effects protects for pulmonary effects and mortality. Liver effects were observed in both rats and mice and increased in severity with dose, ranging from increased liver weights and inflammation at lower doses to necrosis at higher doses.

Clinical signs of toxicity that could be neurotoxic and/or agonal were observed at concentrations/dose levels of furfural that cause pulmonary toxicity and mortality by the oral and dermal routes. There was no evidence of qualitative or quantitative susceptibility observed in the developmental rat and rabbit studies or in the 2-generation reproduction study in rats.

In 2013, the Cancer Assessment Review Committee (CARC) re-classified furfural and furfuryl

alcohol (soil degradate of furfural) each as "Likely to Be Carcinogenic to Humans". The CARC recommended the low dose extrapolation method (Q_1*) for quantification of human cancer risk.

Dose Response/Endpoint Selection

Toxicological points of departure (PODs) were selected for inhalation exposures by calculating Human Equivalent Concentrations (HECs) from No Observable Adverse Effect Levels (NOAELs) according to EPA's reference concentration (RfC) methodology (1994). A POD of 40 mg/m^3 for acute inhalation exposure was selected from a special acute inhalation study that showed reversibility of portal-of-entry effects. A POD of 8 mg/m^3 for short-/intermediate-term inhalation exposure was selected from a subchronic inhalation study based on portal-of-entry effects. A systemic HEC is not appropriate since there are no systemic effects identified in either of the inhalation studies. Nasal irritation was the most sensitive portal of entry effect via the inhalation route of exposure. A total uncertainty factor (UF) of 30x (10x for intraspecies variation, and 3x for interspecies variation because the RfC methodology refines the pharmacokinetic component of the composite 10x interspecies factor to 3x) was applied to the HEC to define the air concentration of concern (COC). Therefore, the level of concern (LOC) is for margins of exposure (MOEs) less than 30.

Acute and chronic reference doses (RfDs) were selected for assessment of drinking water exposures. An acute reference dose (aRfD) of 0.8 mg/kg/day for all populations was selected from an acute neurotoxicity (ACN) study based on mortality and changes in Functional Observational Battery (FOB) parameters and decreased motor activity in both males and females seen at 200 mg/kg/day. The total uncertainty factor (UF) is 100 (10X interspecies extrapolation, 10x intraspecies variation). A chronic RfD (cRfD) of 0.1 mg/kg/day for all populations was selected from a chronic feeding study in rats based on pathological effects in the liver (increased incidence of centrilobular necrosis) seen at 30 mg/kg/day (lowest dose tested). An additional 3X uncertainty factor was applied to this study only for extrapolation from a Lowest Observable Adverse Effect Level (LOAEL) to a NOAEL, resulting in a total uncertainty factor of 300x.

A POD of 10 mg/kg/day for short-term incidental oral exposure was selected from a developmental toxicity study in rats based on clinical signs of toxicity (bilateral exopthalmia, tremors, head held low) with a total uncertainty factor of 100x (i.e., LOC is MOE <100).

A POD of 250 mg/kg/day for short-/intermediate-term dermal exposure was selected from a dermal toxicity study based on adverse clinical signs, increased motor activity, and increased mortality with a total uncertainty factor of 100x (i.e., LOC is MOE <100).

Furfural and furfuryl alcohol are both classified as "Likely to be Carcinogenic to Humans". The furfuryl alcohol Q_1*, which is the most potent Q_1*, was used to estimate cancer risk for both furfural and furfuryl alcohol in accordance with CARC policies, with a $Q_1^* = 1.3 \times 10^{-1}$ $(mg/kg/day)^{-1}$.

Dietary Exposure Estimates

The proposed and currently registered uses of furfural are considered non-food, therefore, the

dietary exposure assessment includes drinking water only. Acute, chronic, and cancer dietary [drinking water only] exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16. This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The acute dietary exposure analysis is based on residues in drinking water only. The most highly exposed population subgroup is All Infants (<1 year old) which utilizes <1% of the aRfD. The risk estimates for the general U.S. population and all other regulated population subgroups are below HED's level of concern (<1% of the aRfD). The chronic dietary exposure analysis is based on residues in drinking water only. The most highly exposed population subgroup is All Infants (<1 year old) which utilizes <1% of the cRfD. The risk estimates for the general U.S. population and all other regulated population subgroups are below HED's level of concern (<1% of the cRfD). The cancer dietary assessment made use of the same input assumptions as the chronic analysis. The cancer risk estimate to the U.S. population is 1.7×10^{-6}.

Residential Exposure Estimates

There are no registered or proposed homeowner uses for furfural, however, post-application exposure is possible for recreational activities on treated turf (i.e., athletic fields and golf courses). Although chemical-specific turf transferrable residue (TTR) data are not available, data from a dislodgeable foliar residue (DFR) study on ornamentals were used to estimate surrogate turf residues, and are considered protective because DFR is generally higher than TTR. The DFR were found to decline to negligible levels within 4 hours of application (i.e., 0.00297 $\mu g/cm^2$ compared to the LOQ of 0.00135 $\mu g/cm^2$). Therefore, post-application exposure to furfural residues on treated athletic fields/golf courses is expected to be negligible for recreational athletes/golfers, and a quantitative assessment was not conducted.

Aggregate Exposure Scenarios and Risk Conclusions

While there is a common effect identified in the toxicity studies selected to assess incidental oral and dermal exposure (neurotoxicity), post-application exposure to furfural residues is expected to be negligible based on the results of the DFR study. Therefore, an aggregate exposure assessment was not conducted.

Non-Occupational Bystander Exposure

Non-occupational bystander inhalation exposure is possible for individuals nearby the application sites. A field volatility study of shank injection application to bare soil (MRID# 48708401) was submitted to support the proposed use. In addition, data from the previously-submitted field volatility study conducted on turf in Florida (MRID# 48252901) were used to reassess the currently registered uses. Flux values were estimated from these data and input into the Probabilistic Exposure and Risk model for Fumigants (PERFUM) for use in estimating air concentrations and buffer zones for bystander inhalation exposure. The term "buffer zone" equates to the distance downwind at which a specific concentration of concern or COC (i.e., HEC/UF, which corresponds to an MOE of 30) is met, based on the desired statistical

parameters.

For the whole field distribution, a 75th percentile buffer zone will result in air concentrations that will not exceed the COC along 75% of the total combined buffer zone perimeters for all applications. Note that this does not mean that whole field buffer zones are protective along the buffer zone perimeter in 75% of applications; therefore, they cannot be considered to provide any defined level of protection for individual applications. The term "buffer zone" does not imply any regulatory decision; in the context of this risk assessment, it is defined as the predicted distance for a specific COC.

The bystander inhalation assessment indicates that when 1-acre of turf has been treated, which represents golf course spot treatment, the whole field distribution 75th percentile MOEs range from 42 to 56 at the proposed buffer zone on the label (i.e., a distance of 5 meters from the edge of the treated area). The associated cancer risk estimates range from 3.1E-5 to 4.2E-5 at that distance. For 3 acres of treated turf, representing an athletic field or sod farm treatment, the 75th percentile MOEs range from 35 to 44 at the proposed buffer zone of 15 meters; associated cancer risk estimates range from 4.0E-5 to 5.1E-5. For ornamentals, the label states a maximum treatment area of 10 acres, for which 75th percentile MOEs range from 28 to 35 at the proposed buffer zone, with associated cancer risk estimates ranging from 5.1E-5 to 7.7E-5; the proposed buffer zone for a 5-acre ornamental treatment yields MOEs ranging from 27 to 37, and cancer risks ranging from 6.3E-5 to 8.5E-5. Although bare ground applications are proposed to field sizes up to 40 acres, because furfural is applied via shank injection or chemigation beneath tarps, the resulting air concentrations are relatively low; the 75th percentile MOEs at the proposed buffer zone range from 159 to 232; the associated cancer risks range from 1.3E-6 to 1.8E-6. Note that the previously summarized cancer risks are estimated using standard amortization factors including an assumed 50 years of exposure out of a 78-year lifetime. As requested by the Registration Division, additional cancer risk estimates were calculated using the time-limited exposure durations of 10 years for currently registered uses and 5 years for the proposed use; these cancer risk estimates are provided in an appendix to this document.

Occupational Exposure Estimates

Handler

The results of the handler occupational exposure and risk assessment indicate that dermal non-cancer risk estimates are not of concern (i.e., MOEs greater than the LOC of 100) when gloves are worn for mixing/loading; which are required on the proposed label for all handlers. The dermal MOEs range from 33 (190 with gloves) to 1,400. Inhalation MOEs range from 270 to 5,700 without a respirator, and therefore, are not of concern. However, cancer risk estimates at the maximum levels of mitigation (gloves, coveralls and a respirator, or engineering controls) for private owners/growers range from 9E-6 to 5E-5; for commercial operators the cancer risk estimates range from 3E-5 to 2E-4.

Post-application

The bystander inhalation assessment (summarized previously) is protective of occupational post-application inhalation exposure. The whole field distribution 75th percentile MOEs for the various field sizes range from 27 to 230 at the label-proposed buffer zones (5 to 15 meters); the

LOC is for MOEs less than 30. The corresponding cancer risk estimates range from 1.3E-6 to 8.5E-5.

For dermal exposure, the results of the DFR study (discussed previously) indicate that furfural residues decline to negligible levels within 4 hours of application. Therefore, occupational post-application exposure to furfural residues on treated turf is expected to be negligible, and a quantitative assessment was not conducted. The furfural technical material has been classified in Toxicity Category III for acute dermal toxicity (reclassification D383688, B. Hanson, 12/16/10), Category IV for acute dermal irritation, and Category II for primary eye irritation. Per the Worker Protection Standard (WPS), a 24-hr restricted entry interval (REI) is required for chemicals classified under Toxicity Category II and a 12-hr REI is required for chemicals classified under Toxicity Category III and IV. The proposed furfural label indicates an REI of 12 hours, which is adequate given the results of the DFR study. This product is proposed for use on bare ground as a pre-plant application for agricultural crops, and is registered for use on outdoor ornamentals, sod and seed farms, which are within the scope of the WPS, therefore, the REI on the label is appropriate. Furfural is also registered for use on athletic fields and golf courses, to which the WPS does not apply; the label correctly contains language cautioning unprotected persons to keep out of treated areas until sprays have dried.

Use of Human Studies

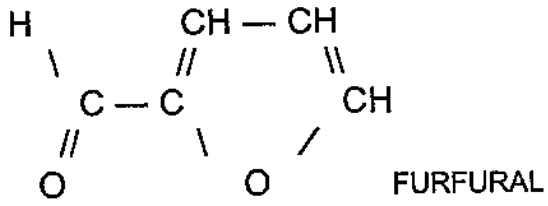
This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from PHED 1.1; the AHETF database; the Outdoor Residential Exposure Task Force (ORETF) database and the ARTF database, are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[1].

2. PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Furfural is a by-product of sugar cane processing. The nomenclature and chemical structure of furfural are shown below:

Common name:	Furfural Technical
IUPAC name:	2-Furaldehyde or furfural
CAS name:	2-Furancarboxaldehyde
CAS #:	98-01-01

1 http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure



2.1. Physical and Chemical Properties

The product chemistry data for furfural were reviewed by the Registration Division (D295324, 2/26/04, L. Kutney). Furfural is an oily liquid with an almond-like odor characteristic of aldehydes. It is yellow in color, turning reddish-brown to black on exposure to air.

Molecular Weight:	96.1 g/mol
Boiling point:	161.7°C
Density:	1.16g/mL at 20°C
Water solubility (20°C):	7.81 g/100 mL
Solvent solubility (mg/L at 20°C):	alcohol (infinite) ether (infinite) miscible in octanol, acetone, xylene, ethyl acetate, methylene chloride and methanol
Vapor pressure:	2.6 mm Hg (at 20°C)
Dissociation constant (pK_a):	Does not demonstrate a dissociation constant between pKa2 and pKa10.
Octanol/water partition coefficient Log(K_{OW}):	0.35 at 20°C
UV/Visible absorption:	14591.3 cm^2/mole (pH 7) 15324.2 cm^2/mole (pH 1.94) 14584.8 cm^2/mole (pH 10.12)

3. HAZARD CHARACTERIZATION AND DOSE-RESPONSE ASSESSMENT

3.1. Toxicology Studies Available for Analysis

The hazard database for furfural is complete. The toxicity database consists of single- and repeated-dose animal toxicity studies from the open literature that use various species and various routes of exposure as well as several studies conducted according to agency guidelines (See Appendix A). The previously required studies, which included acute neurotoxicity (MRID 48998502), 2-generation reproduction toxicity (MRID 49139201), and immunotoxicity (MRID 48999301) studies, have been submitted, reviewed, and found to be acceptable. The requirement of a subchronic neurotoxicity study has been waived by the HASPOC (TXR No. 0056939). This approach considered all of the available hazard and exposure information for furfural including: 1) The oral acute neurotoxicity (ACN) resulted in systemic effects at high doses (200 mg/kg); 2) the inhalation studies suggest portal-of-entry effects are more sensitive than systemic effects; 3) the PODs for risk assessment are protective of neurotoxicity when considering the shorter duration of exposure associated with relatively rapid dissipation due to volatilization and degradation and 4) a subchronic neurotoxicity study, either oral or inhalation, will not likely provide a lower POD or a more sensitive endpoint for the risk assessment.

3.2. Absorption, Distribution, Metabolism, and Elimination (ADME)

No guideline metabolism studies are available for furfural. However, a study was identified in the open scientific literature that is considered acceptable for regulatory use. In this study, furfural administered via gavage (in corn oil) was rapidly absorbed and excreted, with about 80% of the elimination occurring within 24 hours. The major route of excretion was in the urine, in which 85% (out of a total recovered dose of 90%) was found by 72 hours. There were no changes in excretion indicative of saturation of excretion with increasing dose. Expired radioactivity (as carbon dioxide) was a minor route of excretion at 6.6% and was measured for the high dose only. The feces were also a minor route of excretion at ≤2% of the administered dose. Furfural was retained in tissues at low levels of less than 1% of the administered dose (range 0.1 ± 0.1% at 0.127 mg/kg to 0.6 ± 0.1% at 12.5 mg/kg), indicating low potential for bioaccumulation.

Furoylgylcine was the major urinary metabolite for both the high and low dose groups, comprising over 75% of urinary metabolites by 48 hours. Furoic acid and furanacrylic acid were minor urinary metabolites that were present at <5% after 48 hours. The average levels of unidentified urinary metabolites were low, at less than 2%.

These results support a metabolic pathway in which furfural is converted to furanacrylic acid (presumably by condensation with acetyl-CoA), which is excreted in the urine (a minor pathway) or oxidized to furoic acid (the major pathway). Furoic acid can be excreted unchanged in the urine (a minor pathway), decarboxylated and exhaled as carbon dioxide (a minor pathway), or conjugated with glycine to form furoylglycine, which is excreted in urine (the major pathway).

Dermal Absorption

A 28-day dermal toxicity study in rats was used for the dermal endpoint.

No dermal absorption studies for furfural are available. However, there is a need for a dermal absorption factor for the occupational handler cancer assessment. Since there are no dermal absorption data, a dermal absorption value was estimated by doing a comparison between repeat oral dose and repeat dermal dose toxicity studies which have similar treatment durations, species, and toxicities. In this case, the maternal LOAEL of 50 mg/kg/day from the developmental toxicity study in rats (based on clinical signs, including exopthalmia, tremors and head held low) was divided by the LOAEL of 500 mg/kg/day from the dermal toxicity study in rats (mortality, increased motor activity, hypothermia, hypoactivity and hindlimb immobility). The derived dermal absorption factor (DAF) is 10%. [Oral LOAEL/dermal LOAEL, (50/500 mg/kg/day) x 100% = 10%]. This dermal absorption factor is considered health protective since the dermal equivalent dose for the developmental rat study is 500 mg/kg/day (LOAEL of 50/10% DAF), which is the same as the dermal LOAEL.

3.3. Toxicological Effects

Inhalation exposure to furfural vapor in rats results in respiratory effects, both at the portal of entry (the nose) and in the deep lung (pulmonary effects) following both acute and repeated exposures. The portal-of-entry effects (e.g. nasal inflammation as indicated by infiltration of inflammatory cells, hyperplasia, and degeneration) occur at lower concentrations than the pulmonary effects (breathing abnormalities that can progress to mortality at high doses), and so protecting for portal-of-entry effects protects for pulmonary effects. Importantly, portal-of-entry effects of low severity (e.g. slight nasal inflammation) that occur after a single exposure are completely reversible within 2 weeks.

Exposure to furfural via the oral and dermal routes also results in pulmonary toxicity indicative of respiratory distress, which likely mediates the mortality observed at high dose levels of furfural. For the oral route only, liver toxicity is also observed, but at lower doses than those that cause pulmonary toxicity, and so protecting for liver effects protects for pulmonary effects and mortality. Liver effects were observed in both rats and mice and increased in severity with dose, ranging from increased liver weights and inflammation at lower doses to necrosis at higher doses.

Clinical signs of toxicity that could be neurotoxic and/or agonal are also observed at concentrations/dose levels of furfural that cause pulmonary toxicity and mortality by the oral and dermal routes. Maternal animals in the developmental rat toxicity study exhibited clinical signs suggestive of neurotoxicity during daily examinations. These signs included tremors and head held low, hypoactivity, vocalization, prostrate animals, lethargy, limited use of hind limbs and unkempt appearance. This occurred in the context of respiratory toxicity (labored respiration, rales and gasping, rapid respiration). There were also indications of neurotoxicity (drowsiness, dyspnea, clonic convulsions, hyperactivity, tremor, and vocalization) in the 28-day dermal toxicity study that occurred at doses that cause pulmonary toxicity. The range-finding ACN and main ACN study results suggest that toxicity was not observed until significantly higher doses were reached.

There was no evidence of qualitative or quantitative susceptibility seen in the oral gavage developmental rat and rabbit studies or in the gavage two-generation reproduction study in rats. Developmental toxicity studies indicate that any developmental toxicity resulting from furfural would be secondary to maternal toxicity. This is supported by a study in rabbits in which developmental toxicity was limited to decreased body weight at dose levels that caused decreased body weight in maternal animals, and a study in rats in which no developmental toxicity was observed at dose levels that caused maternal toxicity (clinical signs). No parental, reproductive or offspring effects were observed in the 2-generation reproduction study up to the highest dose tested (60 mg/kg/day).

3.4. Consideration of Toxicity to Children

Since there are no currently registered food uses and no tolerances for furfural, furfural is not subject to the Food Quality Protection Act (1996). Therefore, for the purposes of the furfural risk assessment, an FQPA assessment is not included.

3.5. Toxicity Endpoint and Point of Departure Selections

3.5.1. Dose-Response Assessment

Toxicity endpoints and points of departure (PODs) for acute and chronic dietary (water) and occupational/residential exposure scenarios are summarized below. A detailed description of the studies used as a basis for the selected endpoints are presented in Appendix A.

An acute reference dose (RfD) for all populations of 0.8 mg/kg/day was selected from an acute neurotoxicity (ACN) study with a NOAEL of 80 mg/kg/day. The LOAEL of 200 mg/kg/day is based on mortality and changes in Functional Observational Battery (FOB) parameters and decreased motor activity in both males and females. This study is appropriate for the acute dietary endpoint for the general population since the effects occurred following a single oral dose. *(Note: This study/endpoint replaces the previous acute dietary endpoint in the 2012 risk assessment which was based on conservative effects in a developmental rat study which were determined not to be the result of a single exposure (D419653, 9/23/2014)).* Based on the submission of an acceptable/guideline ACN study, there is no longer a data gap, and the 10X database uncertainty factor may be removed. The total uncertainty factor is 100 (10X intraspecies variation, 10X interspecies extrapolation).

The remaining endpoints have not changed since the 2012 risk assessment (See Appendix A). A chronic RfD of 0.1 mg/kg/day for all populations was selected from a LOAEL in a chronic feeding study in rats based on pathological effects in the liver (increased incidence of centrilobular necrosis and cystic degeneration). An additional uncertainty factor of 3X was added to this study only to account for extrapolation from a LOAEL to a NOAEL. A 3X is considered protective because the incidence of centrilobular necrosis of the liver was approximately 3-fold greater at the LOAEL compared to controls, indicating that the NOAEL lies within a 3-fold range of the LOAEL. The total uncertainty factor is 300 (10X intraspecies variation, 10X interspecies, 3X LOAEL to NOAEL extrapolation).

A POD for short-term incidental oral exposure was selected from a developmental toxicity study in rats (NOAEL = 10 mg/kg/day) based on clinical signs of toxicity (bilateral exopthalmia, tremors, head held low) seen at 50 mg/kg/day. The residential level of concern for MOE is 100X.

A POD for short-/intermediate-term dermal exposure was selected from a dermal toxicity study (NOAEL = 250 mg/kg/day) based on adverse clinical signs, increased motor activity, and increased mortality seen at 500 mg/kg/day. The residential and occupational levels of concern for MOE is 100.

PODs for inhalation exposures were selected by calculating Human Equivalent Concentrations (HECs) from NOAELs according to EPA's reference concentration (RfC) methodology (1994); more detail on the derivation of the HECs can be found in Appendix B. A POD of 40 mg/m^3 for acute inhalation exposure was selected from a special acute inhalation study that showed reversibility of portal-of-entry effects. A POD of 8 mg/m^3 for short-/intermediate-term inhalation exposure was selected from a subchronic inhalation study based on portal-of-entry effects. The residential and occupational levels of concern for post-application inhalation exposure is an MOE of 30 route (10X for intraspecies variation, and 3x for interspecies variation because the RfC methodology refines the pharmacokinetic component of the composite 10X interspecies factor to 3X). For occupational handler exposure, the LOC is for an MOE of 100 because the RfC methodology was not employed when converting the concentration units of mg/m^3 to dose units of mg/kg/day.

All data gaps have now been satisfied and the 10X database uncertainty factor has been removed for the oral and dermal scenarios.

3.5.2. Recommendation for Combining Routes of Exposures for Risk Assessment

For furfural, the dermal and incidental oral LOAELs are based on neurotoxic-like effects. The inhalation LOAEL, however, is based on nasal histopathology and should not be aggregated with oral and dermal. The chronic dietary endpoint is based on liver effects and should not be aggregated with incidental oral, dermal or inhalation.

Cancer Classification and Risk Assessment Recommendation

Since the time of the 2012 risk assessment, the Cancer Assessment Review Committee (CARC) determined furfural and furfuryl alcohol (soil degradate of furfural) both to be individually classified as "Likely to Be Carcinogenic to Humans" (TXR No. 0056891). Furfural was given this classification based on cholangiocarcinoma[2] of the liver, a rare tumor type, observed in male rats, liver tumors in male and female mice, and hepatocellular neoplasms in each sex of mice with compounds structurally very similar to furfural. Furfuryl alcohol's classification was based on nasal tumors in male rats and kidney tumors in male mice. The CARC recommended the low

[2] Note: The registrant submitted a Pathology Working Group (PWG) re-read of the cholangiocarcinomas in male rats given furfural and identified them as non-neoplastic. Since mode of action (MOA) studies for the furfuryl alcohol tumors are currently on-going, a CARC meeting will be held when all the data are reviewed.

dose extrapolation method (Q_1*) for quantification of human cancer risk[3]. The most potent oral slope factor [Q_1* (mg/kg/day)$^{-1}$], of furfuryl alcohol, based upon male rat nasal combined tumor rates, is 1.31 x 10^{-1} (mg/kg/day)$^{-1}$ [or 2.497 (µg/m^3)$^{-1}$] in human equivalents (TXR No. 0056959). The most potent unit risk, Q_1* (mg/kg/day)$^{-1}$ of furfural based on male mouse liver combined tumor rates is 3.49x10^{-2} in human equivalents (TXR No. 0056864).

Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Table 3.5.2.1: Summary of Toxicological Doses and Endpoints for Furfural for Use in Dietary and Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (general population)	NOAEL = 80 mg/kg/day	UF_A= 10x UF_H=10x Total UF = 100	Acute RfD = 0.8 mg/kg/day	Acute Neurotoxicity Study Rat (MRID 48998502) LOAEL = 200 mg/kg/day based on effects on mortality, changes in FOB parameters, and decreased motor activity in males and females.
Chronic Dietary (All Populations)	LOAEL = 30 mg/kg/day	UF_A= 10x UF_H=10x UF_L = 3X (LOAEL to NOAEL extrapolation) Total UF=300	Chronic RfD = 0.1mg/kg/day	Chronic Rat (MRID 46011016) Systemic Toxicity LOAEL = 30 mg/kg/day based on liver pathological observations (centrilobular necrosis and cystic degeneration). NOAEL not established.
Incidental Oral Short-Term (1-30 days) and Intermediate Term (1-6 months)	NOAEL= 10 mg/kg/day	UF_A= 10x UF_H=10x	Residential LOC for MOE = 100 (This is also applicable to the young)	Developmental Rat (MRID 46147601) Maternal LOAEL = 50 mg/kg/day based on clinical signs of toxicity (one hour post-dosing, bilateral exophthalmia, tremors, and head held low).

[3] Mode of action studies are currently being developed by the registrant for the tumor types seen in animals treated with furfural or furfuryl alcohol.

Table 3.5.2.1: Summary of Toxicological Doses and Endpoints for Furfural for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short-Term (1-30 days) and Intermediate-Term (1- 6 months)	NOAEL = 250 mg/kg/day	UF_A=10x UF_H=10x	Residential LOC for MOE = 100	28-Day Dermal Rat (MRID 46917201; 46917202) **Systemic Toxicity** LOAEL = 500 mg/kg/day, based on adverse clinical signs (males), an increase in motor activity (males) and increased mortality (males and females).
Inhalation Acute	Port-of-entry NOAEL = 40 mg/m^3 (HDT) Bystander HEC = 6.63 mg/m^3	UF_A=3x UF_H=10x	Residential LOC for MOE = 30	Acute Inhalation Rats (MRID 48563701) LOAEL not observed. (At ≥20 mg/m^3, very slight/slight nasal lesions in males rats were fully reversible within 2 weeks of a single exposure.)
Inhalation Short-Term (1-30 days) and Intermediate-Term (1- 6 months)	Port-of-entry NOAEL = 8 mg/m^3 Bystander HEC = 0.95mg/m^3	UF_A=3x UF_H=10x	Residential LOC for MOE = 30	28-Day Inhalation Rats (MRID 47419101) Port-of-entry LOAEL = 20 mg/m^3 based on nasal epithelial pathology seen throughout all of the treated animal groups.
Cancer (oral, dermal, inhalation)	Furfural and Furfuryl Alcohol were both classified by CARC as "Likely to Be Carcinogenic to Humans" with Q_1*'s (TXR No. 0056891, 2/6/2014). The most potent oral slope factor [Q_1* $(mg/kg/day)^{-1}$], of furfuryl alcohol, based upon male rat nasal combined tumor rates, is 1.31×10^{-1} $(mg/kg/day)^{-1}$ [or 2.497 $(\mu g/m^3)^{-1}$] in human equivalents (TXR No. 0056959). The most potent unit risk, Q_1* $(mg/kg/day)^{-1}$ of furfural based on male mouse liver combined tumor rates is 3.49×10^{-2} in human equivalents (TXR No. 0056864).			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. HDT = highest dose tested. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Table 3.5.2.2: Summary of Toxicological Doses and Endpoints for Furfural for Use in Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short-Term (1-30 days) and Intermediate-Term (1- 6 months)	NOAEL = 250 mg/kg/day A dermal absorption estimate of 10% was used to estimate cancer risk.	UF_A=10x UF_H=10x	Occupational LOC for MOE = 100	28-Day Dermal Rat (MRID 46917201; 46917202) **Systemic Toxicity** LOAEL = 500 mg/kg/day, based on adverse clinical signs (males), an increase in motor activity (males) and increased mortality (males and females).
Inhalation Acute	Port-of-entry NOAEL = 40 mg/m^3 (HDT) Occupational HEC = 6.63 mg/m^3	UF_A=3x UF_H=10x	Occupational LOC for MOE = 30	Acute Inhalation Rats (MRID 48563701) No LOAEL. (At ≥20 mg/m^3, very slight/slight nasal lesions in males rats were fully reversible within 2 weeks of a single exposure.).
Inhalation Short-Term (1-30 days) and Intermediate-Term (1- 6 months)	Port-of-entry NOAEL = 8 mg/m^3 or 2.09 mg/kg/day[1]	UF_A=10x UF_H=10x	Occupational LOC for MOE = 100	28-Day Inhalation Rats (MRID 47419101) Port-of-entry LOAEL = 20 mg/m^3 based on nasal epithelial pathology seen throughout all of the treated animal groups.
Cancer (oral, dermal, inhalation)	Furfural and Furfuryl Alcohol were both classified by CARC as "Likely to Be Carcinogenic to Humans" with Q_1*'s (TXR No. 0056891, 2/6/2014). The most potent oral slope factor [Q_1* $(mg/kg/day)^{-1}$], of furfuryl alcohol, based upon male rat nasal combined tumor rates, is 1.31 x 10^{-1} $(mg/kg/day)^{-1}$ [or 2.497 $(\mu g/m^3)^{-1}$] in human equivalents (TXR No. 0056959). The most potent unit risk, Q_1* $(mg/kg/day)^{-1}$ of furfural based on male mouse liver combined tumor rates is 3.49x10^{-2} in human equivalents (TXR No. 0056864).			

[1] Inhalation NOAEL = 2.09 mg/kg/day. The dose in mg/L was converted to mg/kg/day using the following equation: Dose (mg/kg/day) = (NOAEL (0.008 mg/L) * Respiration rate of a young adult Sprague-Dawley rat (10.26 L/hr) * Study daily exposure duration (6 hr/day)) / Body weight of a young adult Sprague-Dawley rat (0.236 kg).

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

3.6. Endocrine Disruption

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision for furfural, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), furfural is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[4] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website[5].

[4] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

[5] http://www.epa.gov/endo/

4. EXPOSURE ASSESSMENT

4.1. Summary of Proposed/Registered Uses

Furfural is a fungicidal active ingredient (ai) in the proposed end use product MULTIGUARD PROTECT® EC for the control of root infesting plant parasitic nematodes, and fungal plant diseases such as species of *Pythium*, *Phytophthora*, *Fusarium* and *Rhizoctonia*. The proposed and use rates and application methods, as well as those being reevaluated, are summarized in Table 4.1.

Table 4.1. Summary of Use Pattern/Formulation Information

Formulation Type	Application Method	Use Site	Application Rate	Frequency of Application	Application Interval
Furfural MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1) (flowable concentrate) 90% ai (8.68 lb ai/gal)	**Proposed Use**				
	Shank Injection, Chemigation	Bare Soil	69.5 (lb ai/A)	1 pre-plant application (per crop)	Not applicable
	Currently Registered Uses				
	Groundboom	Athletic Fields	47.7 – 69.5 (lb ai/A)	6 applications (per growing season)	14 to 28 days
		Golf Course (tees, greens, spot treatment on fairways and roughs)			
		Sod Farms			
	Chemigation	Outdoor Ornamentals	19.5 – 47.7 (lb ai/A)	4- 8 applications (per crop)	14 to 28 days
	Drench		0.174 – 0.339 (lb ai/100 gal)		7 to 28 days

4.2. Dietary Exposure/Risk Pathway

Reference: Updated Drinking Water Assessment for New Proposed Bare Soil Uses and Existing Uses of Furfural. J. Melendez and G. Rothman, D430230, 12/15/15

Furfural: Acute, Chronic, and Cancer Dietary (Drinking Water Only) Exposure Analysis for the Section 3 Use on Bare Soil. T. Morton, D430684, 6/1/16

Furfural. Non-Food Use Determination. D405498, 11/8/12.

The currently registered (golf courses, sod farms, athletic fields and ornamentals) and proposed (bare soil) use patterns are considered non-food uses (T. Morton, D405498, 11/8/12). However, because of the high application rate of furfural, and the large amounts of water used during and after application, furfural may inadvertently be transported into drinking water sources. Therefore, to be health protective, the HED has conducted a dietary assessment for drinking water only.

4.2.1. Drinking Water Data

The Estimated Drinking Water Concentration (EDWC) used in the dietary risk assessment was provided by the EFED (Memo, D430230, J. Melendez and G. Rothman, 12/15/15). The EDWCs represent the total concentration of furfural and furfuryl alcohol.

The proposed label specifications require the use of tarps concurrent with applications for the new bare soil uses, thus the existing furfural uses with untarped applications to turf (e.g., sod farms, athletic fields, and golf course tees and greens, fairways, and roughs) result in the highest exposure to drinking water sources. Therefore, the drinking water assessment for the existing registered uses on turf is re-evaluated in this memo considering additional information on furfural's biodegradation half-lives in soil from new aerobic soil metabolism studies (MRID No. 49583601), and supersedes the original ***Turf and Ornamentals DWA*** (DP Barcode D371160, dated 12/10/2009). EDWCs evaluated in Using the Tier 1 model FIRST (surface water) and the Pesticide in Water Concentration (PWC v.1.39, ground water) model, it was found that the highest acute estimated drinking water concentrations (EDWCs) occur in surface water sources, but the highest chronic and cancer exposure occurs in ground water sources. The FIRST acute EDWC in surface water is **14.5 ppb**. The chronic and cancer EDWC in ground water is **0.622 ppb**, based on the WI Sand Scenario of the PWC (**Table 4.2.1**). This drinking water exposure assessment included all total toxic residues of concern identified which include furfural and its degradate furfuryl alcohol. EDWCs in this assessment are lower than all of the previous drinking water assessments mainly due to shorter half-lives found in newly submitted aerobic soil metabolism studies for furfural.

Additional information concerning the water models is available at the EPA internet site: http://www.epa.gov/oppefed/models/water/.

Table 4.2.1. Maximum Estimated Drinking Water Concentrations (EDWCs) for the new proposed bare soil uses and existing uses of Furfural and the corresponding driving drinking water source for risk.				
Exposure Duration	**Driving Drinking Water Source for Risk**	**Furfural Use and Application Method, Max. Application Rate, # Apps., Min. Application Interval**	**Model and Scenario**	**EDWC (ppb)[1]**
Acute	Surface Water (Reservoir)	Spray Chemigation to Turf (e.g., Sod Farms, Athletic Fields, Golf Course Tees and Greens, Fairways, and Roughs) 69.4 lbs. a.i./A, 6 apps., 14 days apart	FIRST (Index Reservoir)	14.5
Chronic and Cancer	Ground Water (Well)		PRZM-GW (WI Sands)	0.622

[1]EDWCs presented include the TTRs of furfural and furfuryl alcohol.

4.2.2. Acute and Chronic Drinking Water Exposure

Acute, chronic, and cancer dietary [drinking water only] exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16. This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The acute dietary exposure analysis is based on residues in drinking water only. The most highly exposed population subgroup is All Infants (<1 year old) which utilizes <1% of the aRfD. The risk estimates for the general U.S. population and all other regulated population subgroups are below HED's level of concern (<1% of the aRfD). The chronic dietary exposure analysis is based on residues in drinking water only. The most highly exposed population subgroup is All Infants (<1 year old) which utilizes <1% of the cRfD. The risk estimates for the general U.S. population and all other regulated population subgroups are below HED's level of concern (<1% of the cRfD). The cancer dietary assessment made use of the same input assumptions as the chronic analysis. Furfural and furfuryl alcohol are both classified as "Likely to be Carcinogenic to Humans". The furfuryl alcohol Q_1* was used to estimate cancer risk, with a $Q_1^* = 1.3 \times 10^{-1}$ $(mg/kg/day)^{-1}$. The cancer risk estimate to the U.S. population is 1.7×10^{-6}.

Table 4.2.2. Summary of Dietary Exposure and Risk for Furfural (Drinking Water Only)						
	Acute Dietary 95th percentile		Chronic Dietary		Cancer	
Population Subgroup*	Dietary Exposure (mg/kg/day)	% aRfD	Dietary Exposure (mg/kg/day)	% cRfD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	0.000791	<1	0.000013	<1	0.000013	$1.7x10^{-6}$
All Infants (< 1 year old)	**0.002476**	**<1**	**0.000034**	**<1**		
Children 1-2 years old	0.001219	<1	0.000019	<1		
Children 3-5 years old	0.000989	<1	0.000016	<1		
Children 6-12 years old	0.000756	<1	0.000011	<1		
Youth 13-19 years old	0.000658	<1	0.000009	<1		
Adults 20-49 years old	0.000778	<1	0.000013	<1		
Adults 50-99 years old	0.000693	<1	0.000013	<1		
Females 13-49 years old	0.000789	<1	0.000013	<1		

The bolded %RfD is the highest exposure.

4.3. Residential Exposure

There are no registered or proposed residential uses for furfural, however, post-application exposure is possible for recreational activities on treated turf (i.e., athletic fields and golf courses). The registrant did not submit a chemical-specific turf transferrable residue (TTR) study for use in assessing post-application dermal exposure, however, a dislodgeable foliar residue (DFR) study on ornamentals (MRID#: 47146202) was provided previously (summarized in D389907, K. O'Rourke, 8/8/2012). These DFR data were used to estimate surrogate turf residues, and are considered protective because DFR are generally higher than TTR.

Although the use pattern indicates a potential for post-application contact with furfural residues on treated athletic fields/golf courses, DFR/TTR were found to decline to negligible levels within 4 hours of application (i.e., 0.00297 µg/cm^2 compared to the LOQ of 0.00135 µg/cm^2), and exposure via these scenarios is expected to be negligible. Therefore, quantitative dermal and incidental ingestion assessments were not conducted.

4.4. Aggregate Risk Assessments and Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

As discussed previously, for furfural, the dermal and oral LOAELs are based on neurotoxicity-like effects. The inhalation LOAEL, however, is based on nasal histopathology and should not be aggregated with oral and dermal.

While there is a common effect in the toxicity studies selected to assess oral and dermal exposure (neurotoxicity), post-application exposure to residues is expected to be negligible based on the results of the DFR study. Therefore, an aggregate exposure assessment was not conducted.

5. NON-OCCUPATIONAL BYSTANDER EXPOSURE

Reference: *Furfural. Review of "Monitoring of Flux from Soil Injection/Rotovation Application Method of Multiguard Protect® (90% Furfural as active ingredient) on Bare Ground Applications in Florida". EPA PC Code: 043301.* K. O'Rourke (HED) and G. Rothman (EFED), D404858, 2/25/2016.

Furfural. Review of "Monitoring of the Flux from the Surface Spray Application of Multiguard Protect® EC (90% Furfural as active ingredient) on Established Turf in Fort Pierce, Florida". EPA PC Code: 043301. K. O'Rourke (HED) and G. Rothman (EFED), D384958, 3/29/12.

5.1. Spray Drift Exposure and Risk Estimates

Spray drift is a potential source of exposure to those nearby pesticide applications. This is particularly the case with aerial application, but, to a lesser extent, spray drift can also be a potential source of exposure from the ground application methods (e.g., groundboom) employed for furfural**.** The agency has been working with the Spray Drift Task Force (a task force composed of various registrants which was developed as a result of a Data Call-In issued by EPA), EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices (see the agency's Spray Drift website for more information: http://www2.epa.gov/reducing-pesticide-drift). The agency has also developed a policy on how to appropriately consider spray drift as a potential source of exposure in risk assessments for pesticides. The potential for spray drift will be quantitatively evaluated for each pesticide during the *Registration Review* process which ensures that all uses for that pesticide will be considered concurrently. The approach is outlined in the revised (2012) *Standard Operating Procedures For Residential Risk Assessment (SOPs) - Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift.* This document outlines the quantification of indirect non-occupational exposure to drift.

5.2. Bystander Post-Application Inhalation Exposure and Risk Estimates

Non-occupational bystander exposure to furfural may occur because of its volatility, resulting in emissions from treated athletic fields, golf courses, sod farms, ornamental nurseries, and pre-plant bare soil treatments. These emissions can travel via air currents to non-target areas which could lead to negative impacts on human health, and will be referred to simply as bystander risks in this assessment.

Bystander exposure to furfural depends on two main factors – (1) the rate at which furfural comes off of a treated field (described as the emission or flux) and (2) how those resulting furfural emissions are dispersed in the air over and around the field. Furfural emission rates are affected primarily by the amount applied (which is proportional to the rate and area treated), application methods and equipment, irrigation timing, and field conditions (e.g., soil type, temperature, and moisture levels). Soil factors that can potentially have an effect on the magnitude of the concentration of furfural coming off of a treated field include soil type, soil moisture, soil temperature, and organic content of the soil. For example, a higher soil temperature may lead to a greater emission rate, while a higher soil organic content may yield a lower emission rate. In addition, when injected into the soil (e.g., via shank injection, which is the application method proposed for the pre-plant bare soil use) the soil degradation product furfuryl alcohol may be formed.

Once furfural or furfuryl alcohol has been emitted from the field after an application, meteorological conditions and the topography at the site determine how it is dispersed. For example, if winds are high and the atmosphere is unstable, then emitted furfural concentrations are more likely to be reduced as a result of greater mixing. Under such conditions, the likelihood of a bystander being exposed to a concentration of concern (COC) is relatively lower. On the other hand, if winds are light and the atmosphere is stable, then the emitted furfural is more likely to build in concentration, and the likelihood of exposure to a COC is relatively higher.

Topography can also impact wind direction which can impact which individuals are exposed and may actually predispose certain populations to higher exposure levels (e.g., a house located in a valley where prevailing winds approach it).

The Probabilistic Exposure and Risk model for Fumigants (PERFUM) was used in this assessment to evaluate the potential inhalation risks from furfural uses. PERFUM incorporates actual weather data and residue flux distribution estimates, and accounts for changes relative to the time of day and altering conditions. It is also capable of providing distributional outputs for varying receptor locations (i.e., distances downwind from the treated field) and using varied statistical approaches. Additional details regarding the PERFUM outputs is provided in Appendix C.

The term "buffer zone" equates to the distance downwind at which a specific COC (i.e., HEC/UF, which corresponds to an MOE of 30) is met, based on the desired statistical parameters. The use of this term does not imply any regulatory decision. In the context of this risk assessment, it should only be considered as the predicted distance for a specific COC. The COC for furfural is 0.221 mg/m^3 (i.e., bystander HEC/UF = 6.63 mg/m^3/30).

Emission rates, or flux, were determined from available volatility studies. In addition to the field volatility study on turf conducted in Florida (MRID#: 48252901; K. O'Rourke (HED) and G. Rothman (EFED), D384958, 3/29/12), which was used in the previous risk assessment, the registrant submitted a field volatility study on bare ground conducted on a tomato farm, also in Florida (MRID#: 48708401; K. O'Rourke (HED) and G. Rothman (EFED), D404858, 2/25/2016.), to support the proposed use for pre-plant treatment of bare soil. The results of both studies confirm that bystanders could be exposed to concentrations of furfural (and furfuryl alcohol, in the case of the bare soil treatment) in the air after an application. This may occur because emissions coming off of treated fields can travel to non-target areas, which could have adverse impacts on human health. Acute exposure is of concern for bystanders because furfural produces peak emissions in the first few hours after application (117.8 $\mu g/m^2$-s and 5.43 $\mu g/m^2$-s in the first period for relevant turf and bare soil applications, respectively), with fluxes falling below 0.40 $\mu g/m^2$-s within 4 hours in the turf study, and 1.41 $\mu g/m^2$-s in the second period of the bare soil study. The flux profiles for the relevant fields from both studies are presented in Appendix D.

Flux inputs (i.e., field volatility or emissions) for PERFUM calculations were based on the emission profiles developed using the indirect method for the first period of sampling, and the integrated horizontal flux method for the remaining periods.

The flux profile from Field 3 in the Florida turf study was used in calculating the emissions for treated golf courses, athletic fields, sod farms and ornamentals. The analysis was limited to this flux profile because it is the most representative of the potential emissions from these use sites, based on the revised label application instructions (i.e., specification of a maximum spray release height of two feet above the ground with a coarse spray setting or in-ground irrigation systems).

To estimate the emissions for pre-plant bare soil treatments, the Field 1 flux profile from the Florida tomato farm (bare soil) study was used. Although this study also measured air concentrations of furfuryl alcohol, a soil degradate of furfural, the recovery data were

unacceptable; therefore a surrogate method of estimating furfuryl alcohol air concentrations was employed by extrapolating the ratio of furfuryl alcohol to furfural detected in the soil samples (up to 30% of parent), and adjusting the furfural air concentration to reflect the additional contribution of furfuryl alcohol. Because the toxicity endpoints for furfural are considered to be relevant for furfuryl alcohol, the adjusted concentration was compared to the COC and Q*.

Actual meteorological data are integrated into PERFUM for each analysis. The following locations and sources were used in this assessment:

- Bakersfield California (Source: ASOS or Automated Surface Observing System operated by the FAA) to represent inland California locations;
- Ventura California (Source: CIMIS or California Irrigation Management Information System) to represent coastal California locations;
- Flint Michigan (Source: NWS or National Weather Service) to represent central Michigan and other upper midwest locations;
- Tallahassee Florida (Source: NWS or National Weather Service) to represent inland Florida locations;
- Bradenton Florida (Source: FAWN or Florida Automated Weather Network) to represent coastal Florida; and
- Yakima Washington (Source: NWS or National Weather Service) to represent southeastern Washington and other pacific northwest locations.

In this assessment, 5 years or 1825 days of meteorological data were considered in each calculation. Bradenton, Bakersfield, and Ventura data were in the range of 1997 through 2003, the Tallahassee and Flint data were in the late 1980s through early 1990s, and the Yakima data were from 1984-1988.

Buffer zones were estimated for the 6 meteorological regions for several field sizes ranging from one acre to 40 acres. The range in field sizes is provided to bracket the proposed and currently registered use patterns. For golf courses the label indicates that spot treatment is limited to not more than one contiguous acre. Athletic fields were assumed to be within sports complexes estimated to be 3 acres; this was also assumed to be the treated area for sod farms (reduced on the proposed label to spot treatment only, up to 3 contiguous acres). The proposed label limits field-grown ornamental and bare soil treatments to maximum areas of 10 and 40 acres, respectively, in a 24-hour period.

Although it is possible for individuals living nearby treated areas to be exposed to emissions from the field for the entire day, a 6-hour averaging time was used to calculate the air concentrations for bystanders because flux measurements dropped to negligible levels within this period. This timeframe also matches the duration of the acute inhalation toxicity study on which the COC is based.

Tables 5.2.1 through 5.2.5 present the bystander inhalation MOEs (LOC = MOE of 30) based on the whole field distribution. The corresponding cancer risk estimates are presented in Tables 5.2.6 through 5.2.10. The assessment indicates that when 1-acre of turf has been treated, the whole field distribution 75^{th} percentile (for example) MOEs range from 42 to 56 at the proposed buffer zone on the label (i.e., a distance of 5 meters from the edge of the treated area). The

associated cancer risk estimates range from 3.1E-5 to 4.2E-5 at that distance. For 3 acres of treated turf, representing an athletic field or sod farm treatment, the 75th percentile MOEs range from 35 to 44 at the proposed buffer zone of 15 meters; associated cancer risk estimates range from 4.0E-5 to 5.1E-5. For ornamentals, the label states a maximum treatment area of 10 acres, for which 75th percentile MOEs range from 28 to 35 at the proposed buffer zone (15 meters), with associated cancer risk estimates ranging from 5.1E-5 to 7.7E-5; the proposed buffer zone for a 5-acre ornamental treatment (5 meters) yields MOEs ranging from 27 to 37, and cancer risks ranging from 6.3E-5 to 8.5E-5. Although bare ground applications are proposed to field sizes up to 40 acres, because furfural is applied via shank injection or chemigation beneath tarps, the resulting air concentrations are relatively low; the 75th percentile MOEs at the proposed buffer zone range from 159 to 232; the associated cancer risks range from 1.3E-6 to 1.8E-6. The predicted air concentrations at varied distances from treated fields that range from one to 40 acres in size are provided in Appendix E. Tables E1 through E4 are based on the Field 3 flux profile (from the turf study), and Table E5 is based on the Field 1 flux profile from the tomato farm bare soil study. Note that cancer risks are estimated using standard amortization factors including an assumed 50 years of exposure out of a 78-year lifetime. As requested by the Registration Division, additional cancer risk estimates were calculated using the time-limited exposure durations of 10 years for currently registered uses and 5 years for the proposed use; these cancer risk estimates are provided in Appendix F.

Table 5.2.1. MOEs for Varied Distances from a 1-Acre Treated Field – Turf (Golf Course)[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	--
	60	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	70	68	81	114	237	553	3315	3315	3315	3315	3315
	75	44	48	59	85	128	368	3315	3315	3315	3315
	80	33	35	39	48	61	107	368	3315	3315	3315
	85	27	28	30	35	39	56	114	207	301	368
	90	22	23	24	26	29	36	56	85	107	128
Bakersfield	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	70	68	75	92	138	237	829	3315	3315	3315	3315
	75	44	47	52	68	85	158	829	3315	3315	3315
	80	33	33	36	44	52	75	174	553	829	3315
	85	26	26	28	32	36	48	92	158	207	301
	90	21	21	22	24	27	35	54	85	107	128
Bradenton	50	3315	3315	3315	3315	3315	3315	3315	--	--	--
	60	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	70	81	107	158	368	829	3315	3315	3315	3315	3315
	75	42	48	59	92	138	368	3315	3315	3315	3315
	80	28	30	35	44	56	98	301	829	3315	3315
	85	21	22	24	28	33	48	98	174	237	368
	90	16	17	18	20	23	30	50	81	98	114
Flint	50	3315	3315	3315	3315	3315	--	--	--	--	--
	60	3315	3315	3315	3315	3315	3315	3315	3315	--	--
	70	92	107	138	237	553	3315	3315	3315	3315	3315
	75	56	61	72	98	128	301	3315	3315	3315	3315
	80	41	44	47	56	68	107	301	829	3315	3315
	85	33	35	35	39	47	61	107	174	237	301
	90	27	27	29	31	35	44	65	98	114	138
Tallahassee	50	3315	3315	3315	3315	3315	3315	3315	--	--	--
	60	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	70	92	114	174	368	829	3315	3315	3315	3315	3315
	75	52	56	68	98	158	553	3315	3315	3315	3315
	80	37	39	44	52	65	107	368	3315	3315	3315
	85	29	30	32	36	42	56	107	207	301	368
	90	24	24	25	27	30	37	59	85	98	128
Yakima	50	829	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	107	138	207	553	829	3315	3315	3315	3315	3315
	70	54	59	68	92	128	237	3315	3315	3315	3315
	75	44	47	52	65	81	128	368	829	3315	3315
	80	35	37	41	48	56	81	158	301	368	553
	85	30	30	33	37	44	56	92	158	174	237
	90	24	25	27	30	33	42	61	92	107	128

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

MOE = bystander HEC (i.e., = 6630 µg/m^3) / air concentration at given distance (µg/m^3; see Appendix E). The LOC is MOE < 30.

-- indicates concentration estimate is zero for this percentile at this distance.

Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.2. MOEs for Varied Distances from a 3-Acre Treated Field – Turf (Athletic Field/Sod)[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	174	301	553	3315	3315	3315	3315	3315	3315	3315
	70	35	39	47	65	92	237	3315	3315	3315	3315
	75	25	27	30	39	48	75	237	829	3315	3315
	80	21	22	23	27	31	44	81	158	237	368
	85	17	18	19	21	23	29	45	68	81	98
	90	14	14	15	16	17	21	29	39	44	50
Bakersfield	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	207	301	553	3315	3315	3315	3315	3315	3315	3315
	70	35	39	44	54	72	114	553	3315	3315	3315
	75	25	27	29	35	41	59	114	301	553	829
	80	20	21	22	25	29	37	65	107	138	174
	85	16	17	18	19	22	27	41	59	72	85
	90	13	13	14	15	16	20	29	39	45	52
Bradenton	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	368	553	3315	3315	3315	3315	3315	3315	3315	3315
	70	36	42	52	81	128	301	3315	3315	3315	3315
	75	24	26	29	37	48	81	237	829	3315	3315
	80	17	18	20	24	28	39	75	158	207	301
	85	14	14	15	17	19	25	39	61	75	92
	90	11	11	12	13	14	18	25	35	41	48
Flint	50	3315	3315	3315	3315	3315	3315	--	--	--	--
	60	237	368	829	3315	3315	3315	3315	3315	3315	3315
	70	45	48	56	75	107	207	3315	3315	3315	3315
	75	31	33	36	44	52	81	207	553	829	3315
	80	25	26	27	31	35	47	81	138	174	237
	85	21	21	22	24	27	33	48	68	81	98
	90	17	17	18	19	21	25	35	45	52	59
Tallahassee	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	301	553	829	3315	3315	3315	3315	3315	3315	3315
	70	42	47	56	81	128	368	3315	3315	3315	3315
	75	29	30	35	42	52	85	301	3315	3315	3315
	80	22	23	25	29	33	44	81	158	207	301
	85	18	18	19	21	24	29	44	65	75	92
	90	15	15	15	16	18	22	29	39	44	50
Yakima	50	207	301	553	3315	3315	3315	3315	3315	3315	3315
	60	54	61	75	114	174	553	3315	3315	3315	3315
	70	32	35	39	47	56	85	207	553	829	3315
	75	27	28	30	35	42	56	98	174	237	301
	80	22	24	25	29	33	42	65	98	114	138
	85	19	20	21	23	26	32	47	65	72	85
	90	15	16	17	19	20	24	33	45	50	56

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.
MOE = bystander HEC (i.e., = 6630 µg/m^3) / air concentration at given distance (µg/m^3; see Appendix E). The LOC is MOE < 30.
-- indicates concentration estimate is zero for this percentile at this distance.
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.3. MOEs for Varied Distances from a 5-Acre Treated Field – Ornamentals[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	133	184	301	663	3315	3315	3315	3315	3315	3315
	70	39	43	50	65	85	151	663	3315	3315	3315
	75	30	32	35	42	50	72	151	414	663	1105
	80	25	26	28	31	35	46	75	123	166	221
	85	20	21	22	25	27	33	47	65	79	87
	90	17	17	18	19	20	24	32	41	46	51
Bakersfield	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	138	184	237	474	1105	3315	3315	3315	3315	3315
	70	40	43	47	57	69	104	237	1105	3315	3315
	75	30	31	34	39	45	60	104	184	237	414
	80	24	25	26	29	33	41	63	98	123	151
	85	20	20	21	23	26	31	44	60	72	81
	90	16	16	17	18	20	23	32	41	47	53
Bradenton	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	237	332	663	3315	3315	3315	3315	3315	3315	3315
	70	40	45	53	72	104	195	1105	3315	3315	3315
	75	27	29	33	39	49	72	166	414	663	1105
	80	21	22	24	27	31	41	69	114	151	195
	85	17	17	18	20	23	28	41	59	69	81
	90	14	14	14	16	17	21	29	37	43	49
Flint	50	3315	3315	3315	3315	3315	3315	3315	--	--	--
	60	184	237	332	663	3315	3315	3315	3315	3315	3315
	70	50	53	60	75	98	166	474	3315	3315	3315
	75	37	39	41	47	55	79	151	301	414	663
	80	30	31	32	36	39	50	79	114	138	184
	85	25	26	27	29	31	37	53	69	81	92
	90	20	21	22	23	25	29	39	50	55	60
Tallahassee	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	221	301	474	3315	3315	3315	3315	3315	3315	3315
	70	46	50	59	75	104	195	1105	3315	3315	3315
	75	33	35	38	45	53	75	166	414	663	1105
	80	26	27	29	32	37	46	75	114	151	184
	85	21	22	23	25	27	33	46	63	72	85
	90	18	18	18	20	21	25	33	42	47	53
Yakima	50	184	237	332	663	3315	3315	3315	3315	3315	3315
	60	60	68	81	107	151	301	3315	3315	3315	3315
	70	38	40	44	53	63	85	151	301	414	663
	75	32	33	36	41	47	60	98	151	184	221
	80	27	28	30	33	38	46	68	92	107	133
	85	23	24	25	27	30	37	50	68	75	85
	90	19	19	20	22	24	29	38	49	53	59

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.
MOE = bystander HEC (i.e., = 6630 µg/m^3) / air concentration at given distance (µg/m^3; see Appendix E). The LOC is MOE < 30.
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.4. MOEs for Varied Distances from a 10-Acre Treated Field - Ornamentals[1]											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	68	81	107	184	332	1105	3315	3315	3315	3315
	70	29	31	35	42	51	75	184	474	1105	3315
	75	24	25	27	30	35	46	79	133	184	237
	80	20	20	22	24	27	32	47	68	81	98
	85	16	17	18	19	21	25	33	42	47	53
	90	13	13	14	15	16	18	23	29	32	35
Bakersfield	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	72	81	98	151	221	663	3315	3315	3315	3315
	70	30	31	34	39	45	60	107	195	301	414
	75	23	24	26	29	32	40	63	92	114	138
	80	19	20	21	23	25	30	42	59	68	79
	85	16	16	17	18	20	23	31	40	46	53
	90	13	13	14	15	16	18	23	29	32	36
Bradenton	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	104	133	195	414	663	3315	3315	3315	3315	3315
	70	29	31	35	43	53	85	221	663	1105	3315
	75	21	22	24	28	32	43	75	138	184	237
	80	17	17	18	20	23	28	42	60	72	87
	85	14	14	15	16	17	21	29	38	43	49
	90	11	11	12	13	14	16	21	27	29	32
Flint	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	0
	60	92	107	138	221	414	1105	3315	3315	3315	3315
	70	36	38	41	49	57	81	166	414	663	1105
	75	28	29	31	35	39	50	79	123	151	195
	80	24	24	25	27	30	36	50	68	79	92
	85	20	20	21	23	24	28	37	46	53	59
	90	16	17	17	18	20	22	29	35	39	42
Tallahassee	50	3315	3315	3315	3315	3315	3315	3315	3315	3315	3315
	60	98	123	184	332	663	3315	3315	3315	3315	3315
	70	33	35	39	47	57	85	221	663	1105	3315
	75	25	26	28	32	37	47	79	133	184	237
	80	20	21	22	24	27	32	46	65	75	87
	85	17	17	18	19	21	24	32	41	46	51
	90	14	14	15	15	16	19	24	29	32	35
Yakima	50	98	114	151	237	474	3315	3315	3315	3315	3315
	60	45	49	55	69	85	133	332	1105	3315	3315
	70	30	31	34	39	44	57	87	138	166	221
	75	25	26	28	31	35	43	63	87	104	114
	80	21	22	24	26	29	34	46	60	69	79
	85	18	19	20	22	23	27	36	45	50	55
	90	15	15	16	17	19	22	28	34	37	41

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.
MOE = bystander HEC (i.e., = 6630 µg/m^3) / air concentration at given distance (µg/m^3; see Appendix E). The LOC is MOE < 30.
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.5. MOEs for Varied Distances from a 40-Acre Treated Field – Bare Soil[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	2550	2550	2550	2550	2550	2550	2550	2550	2550	2550
	60	425	425	638	638	638	2550	2550	2550	2550	2550
	70	232	232	283	283	425	425	638	2550	2550	2550
	75	182	232	232	283	283	425	638	638	638	2550
	80	182	182	182	232	232	283	425	638	638	638
	85	159	159	182	182	232	232	283	425	425	425
	90	159	159	159	182	182	232	283	283	283	425
Bakersfield	50	638	638	638	638	2550	2550	2550	2550	2550	2550
	60	283	283	283	425	425	638	638	2550	2550	2550
	70	182	182	232	232	283	283	425	638	638	638
	75	159	159	182	182	232	283	425	425	638	638
	80	134	134	159	159	182	232	283	425	425	425
	85	121	121	134	134	159	182	232	283	283	425
	90	106	106	121	121	134	159	182	232	232	283
Bradenton	50	638	638	638	638	2550	2550	2550	2550	2550	2550
	60	283	283	283	425	425	638	638	2550	2550	2550
	70	182	182	232	232	283	283	425	638	638	638
	75	159	159	182	182	232	283	425	425	638	638
	80	134	134	159	159	182	232	283	425	425	425
	85	121	121	134	134	159	182	232	283	283	425
	90	106	106	121	121	134	159	182	232	232	283
Flint	50	2550	2550	2550	2550	2550	2550	2550	2550	2550	2550
	60	425	425	638	638	638	2550	2550	2550	2550	2550
	70	283	283	283	283	425	425	638	638	2550	2550
	75	232	232	232	232	283	283	425	638	638	638
	80	182	182	182	232	232	283	425	425	425	638
	85	159	159	182	182	182	232	283	283	425	425
	90	134	134	159	159	159	182	232	283	283	283
Tallahassee	50	638	638	638	2550	2550	2550	2550	2550	2550	2550
	60	425	425	425	425	638	638	2550	2550	2550	2550
	70	232	232	283	283	425	425	638	638	638	2550
	75	232	232	232	283	283	425	425	638	638	638
	80	182	182	182	232	232	283	425	425	638	638
	85	159	159	182	182	182	232	283	425	425	425
	90	134	134	159	159	182	182	232	283	283	425
Yakima	50	425	425	425	638	638	638	2550	2550	2550	2550
	60	283	283	283	425	425	425	638	2550	2550	2550
	70	232	232	232	283	283	425	425	638	638	638
	75	182	182	182	232	232	283	425	425	638	638
	80	159	159	182	182	232	232	283	425	425	425
	85	134	134	159	159	182	232	283	283	425	425
	90	121	121	121	134	159	159	232	232	283	283

[1] Based on 6-hour average whole field PERFUM run estimated from the Florida tomato farm (bare soil) Field 1 flux profile, with an application rate of 390 lb ai/A. Values presented reflect the total air concentration (i.e., furfural plus furfuryl alcohol) as furfuryl alcohol was found to occur as a soil degradate (up to 30% of parent) when furfural is applied to bare ground.
MOE = bystander HEC (i.e., = 6630 µg/m^3) / air concentration at given distance (µg/m^3; see Appendix E). The LOC is MOE < 30.
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.6. Cancer Risk Estimates for Varied Distances from a 1-Acre Treated Field – Turf (Golf Course)[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--
	60	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	2.6E-05	2.2E-05	1.5E-05	7.4E-06	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	4.0E-05	3.6E-05	2.9E-05	2.1E-05	1.4E-05	4.7E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	80	5.3E-05	5.1E-05	4.5E-05	3.6E-05	2.8E-05	1.6E-05	4.7E-06	5.3E-07	5.3E-07	5.3E-07
	85	6.5E-05	6.3E-05	5.8E-05	5.1E-05	4.4E-05	3.1E-05	1.5E-05	8.4E-06	5.8E-06	4.7E-06
	90	7.8E-05	7.7E-05	7.4E-05	6.8E-05	6.0E-05	4.8E-05	3.1E-05	2.1E-05	1.6E-05	1.4E-05
Bakersfield	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	60	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	2.6E-05	2.3E-05	1.9E-05	1.3E-05	7.4E-06	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	4.0E-05	3.7E-05	3.4E-05	2.6E-05	2.1E-05	1.1E-05	2.1E-06	5.3E-07	5.3E-07	5.3E-07
	80	5.3E-05	5.2E-05	4.8E-05	4.0E-05	3.4E-05	2.3E-05	1.0E-05	3.2E-06	2.1E-06	5.3E-07
	85	6.8E-05	6.6E-05	6.3E-05	5.5E-05	4.8E-05	3.6E-05	1.9E-05	1.1E-05	8.4E-06	5.8E-06
	90	8.5E-05	8.4E-05	7.9E-05	7.3E-05	6.4E-05	5.1E-05	3.2E-05	2.1E-05	1.6E-05	1.4E-05
Bradenton	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--	--	--
	60	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	2.2E-05	1.6E-05	1.1E-05	4.7E-06	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	4.2E-05	3.6E-05	2.9E-05	1.9E-05	1.3E-05	4.7E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	80	6.3E-05	5.8E-05	5.1E-05	4.0E-05	3.1E-05	1.8E-05	5.8E-06	2.1E-06	5.3E-07	5.3E-07
	85	8.4E-05	7.9E-05	7.3E-05	6.3E-05	5.2E-05	3.6E-05	1.8E-05	1.0E-05	7.4E-06	4.7E-06
	90	1.1E-04	1.0E-04	9.8E-05	8.6E-05	7.6E-05	5.7E-05	3.5E-05	2.2E-05	1.8E-05	1.5E-05
Flint	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--	--	--	--	--
	60	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--	--
	70	1.9E-05	1.6E-05	1.3E-05	7.4E-06	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	3.1E-05	2.8E-05	2.4E-05	1.8E-05	1.4E-05	5.8E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	80	4.3E-05	4.0E-05	3.7E-05	3.1E-05	2.6E-05	1.6E-05	5.8E-06	2.1E-06	5.3E-07	5.3E-07
	85	5.2E-05	5.1E-05	4.9E-05	4.4E-05	3.7E-05	2.8E-05	1.6E-05	1.0E-05	7.4E-06	5.8E-06
	90	6.5E-05	6.4E-05	6.1E-05	5.6E-05	5.1E-05	4.0E-05	2.7E-05	1.8E-05	1.5E-05	1.3E-05
Tallahassee	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--	--	--
	60	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	1.9E-05	1.5E-05	1.0E-05	4.7E-06	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	3.4E-05	3.1E-05	2.6E-05	1.8E-05	1.1E-05	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	80	4.7E-05	4.4E-05	4.0E-05	3.4E-05	2.7E-05	1.6E-05	4.7E-06	5.3E-07	5.3E-07	5.3E-07
	85	6.0E-05	5.7E-05	5.5E-05	4.8E-05	4.2E-05	3.1E-05	1.6E-05	8.4E-06	5.8E-06	4.7E-06
	90	7.3E-05	7.3E-05	6.9E-05	6.4E-05	5.7E-05	4.7E-05	2.9E-05	2.1E-05	1.8E-05	1.4E-05
Yakima	50	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	60	1.6E-05	1.3E-05	8.4E-06	3.2E-06	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	3.2E-05	2.9E-05	2.6E-05	1.9E-05	1.4E-05	7.4E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	4.0E-05	3.7E-05	3.4E-05	2.7E-05	2.2E-05	1.4E-05	4.7E-06	2.1E-06	5.3E-07	5.3E-07
	80	4.9E-05	4.7E-05	4.3E-05	3.6E-05	3.1E-05	2.2E-05	1.1E-05	5.8E-06	4.7E-06	3.2E-06
	85	5.8E-05	5.7E-05	5.3E-05	4.7E-05	4.0E-05	3.1E-05	1.9E-05	1.1E-05	1.0E-05	7.4E-06
	90	7.2E-05	6.9E-05	6.5E-05	5.8E-05	5.2E-05	4.2E-05	2.8E-05	1.9E-05	1.6E-05	1.4E-05

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.
Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\ -1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(6 application days/365-day year) x (50 years exposed/78-yr lifetime).
-- indicates concentration estimate is zero for this percentile at this distance.
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.7. Cancer Risk Estimates for Varied Distances from a 3-Acre Treated Field – Turf (Athletic Field/Sod)[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--
	60	1.0E-05	5.8E-06	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	5.1E-05	4.5E-05	3.7E-05	2.7E-05	1.9E-05	7.4E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	6.9E-05	6.4E-05	5.7E-05	4.5E-05	3.6E-05	2.3E-05	7.4E-06	2.1E-06	5.3E-07	5.3E-07
	80	8.5E-05	8.1E-05	7.6E-05	6.5E-05	5.6E-05	4.0E-05	2.2E-05	1.1E-05	7.4E-06	4.7E-06
	85	1.0E-04	9.9E-05	9.4E-05	8.5E-05	7.6E-05	6.0E-05	3.9E-05	2.6E-05	2.2E-05	1.8E-05
	90	1.3E-04	1.2E-04	1.2E-04	1.1E-04	1.0E-04	8.4E-05	6.0E-05	4.5E-05	4.0E-05	3.5E-05
Bakersfield	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--
	60	8.4E-06	5.8E-06	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	4.9E-05	4.5E-05	4.0E-05	3.2E-05	2.4E-05	1.5E-05	3.2E-06	5.3E-07	5.3E-07	5.3E-07
	75	6.9E-05	6.5E-05	6.0E-05	5.1E-05	4.3E-05	2.9E-05	1.5E-05	5.8E-06	3.2E-06	2.1E-06
	80	8.7E-05	8.4E-05	7.8E-05	6.9E-05	6.1E-05	4.7E-05	2.7E-05	1.6E-05	1.3E-05	1.0E-05
	85	1.1E-04	1.0E-04	9.9E-05	9.0E-05	8.1E-05	6.5E-05	4.3E-05	2.9E-05	2.4E-05	2.1E-05
	90	1.3E-04	1.3E-04	1.3E-04	1.2E-04	1.1E-04	8.7E-05	6.1E-05	4.5E-05	3.9E-05	3.4E-05
Bradenton	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--
	60	4.7E-06	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	4.8E-05	4.2E-05	3.4E-05	2.2E-05	1.4E-05	5.8E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	7.4E-05	6.8E-05	6.0E-05	4.7E-05	3.6E-05	2.2E-05	7.4E-06	2.1E-06	5.3E-07	5.3E-07
	80	1.0E-04	9.5E-05	8.7E-05	7.4E-05	6.3E-05	4.5E-05	2.3E-05	1.1E-05	8.4E-06	5.8E-06
	85	1.3E-04	1.2E-04	1.2E-04	1.0E-04	9.0E-05	7.1E-05	4.4E-05	2.8E-05	2.3E-05	1.9E-05
	90	1.6E-04	1.6E-04	1.5E-04	1.3E-04	1.2E-04	9.8E-05	6.9E-05	4.9E-05	4.3E-05	3.6E-05
Flint	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--	--	--	--
	60	7.4E-06	4.7E-06	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	3.9E-05	3.6E-05	3.1E-05	2.3E-05	1.6E-05	8.4E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	5.6E-05	5.2E-05	4.8E-05	4.0E-05	3.4E-05	2.2E-05	8.4E-06	3.2E-06	2.1E-06	5.3E-07
	80	7.1E-05	6.8E-05	6.4E-05	5.6E-05	4.9E-05	3.7E-05	2.2E-05	1.3E-05	1.0E-05	7.4E-06
	85	8.5E-05	8.2E-05	7.8E-05	7.2E-05	6.5E-05	5.3E-05	3.6E-05	2.6E-05	2.2E-05	1.8E-05
	90	1.0E-04	1.0E-04	9.8E-05	9.0E-05	8.4E-05	7.1E-05	5.1E-05	3.9E-05	3.4E-05	2.9E-05
Tallahassee	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--
	60	5.8E-06	3.2E-06	2.1E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	4.2E-05	3.7E-05	3.1E-05	2.2E-05	1.4E-05	4.7E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	75	6.1E-05	5.7E-05	5.1E-05	4.2E-05	3.4E-05	2.1E-05	5.8E-06	5.3E-07	5.3E-07	5.3E-07
	80	7.9E-05	7.6E-05	7.1E-05	6.1E-05	5.3E-05	4.0E-05	2.2E-05	1.1E-05	8.4E-06	5.8E-06
	85	9.8E-05	9.5E-05	9.0E-05	8.2E-05	7.4E-05	6.0E-05	4.0E-05	2.7E-05	2.3E-05	1.9E-05
	90	1.2E-04	1.2E-04	1.1E-04	1.1E-04	9.7E-05	8.1E-05	6.0E-05	4.5E-05	4.0E-05	3.5E-05
Yakima	50	8.4E-06	5.8E-06	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	--
	60	3.2E-05	2.8E-05	2.3E-05	1.5E-05	1.0E-05	3.2E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	5.5E-05	5.1E-05	4.5E-05	3.7E-05	3.1E-05	2.1E-05	8.4E-06	3.2E-06	2.1E-06	5.3E-07
	75	6.5E-05	6.3E-05	5.7E-05	4.9E-05	4.2E-05	3.1E-05	1.8E-05	1.0E-05	7.4E-06	5.8E-06
	80	7.8E-05	7.4E-05	6.9E-05	6.1E-05	5.3E-05	4.2E-05	2.7E-05	1.8E-05	1.5E-05	1.3E-05
	85	9.3E-05	8.9E-05	8.4E-05	7.6E-05	6.8E-05	5.5E-05	3.7E-05	2.7E-05	2.4E-05	2.1E-05
	90	1.1E-04	1.1E-04	1.0E-04	9.4E-05	8.6E-05	7.2E-05	5.2E-05	3.9E-05	3.5E-05	3.1E-05

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.
Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\ -1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(6 application days/365-day year) x (50 years exposed/78-yr lifetime).
-- indicates concentration estimate is zero for this percentile at this distance.
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.8. Cancer Risk Estimates for Varied Distances from a 5-Acre Treated Field – Ornamentals[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	60	1.8E-05	1.3E-05	7.7E-06	3.5E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	5.9E-05	5.4E-05	4.6E-05	3.6E-05	2.7E-05	1.5E-05	3.5E-06	7.0E-07	7.0E-07	7.0E-07
	75	7.7E-05	7.3E-05	6.6E-05	5.5E-05	4.6E-05	3.2E-05	1.5E-05	5.6E-06	3.5E-06	2.1E-06
	80	9.4E-05	9.0E-05	8.4E-05	7.4E-05	6.6E-05	5.1E-05	3.1E-05	1.9E-05	1.4E-05	1.1E-05
	85	1.1E-04	1.1E-04	1.0E-04	9.5E-05	8.5E-05	7.1E-05	4.9E-05	3.6E-05	2.9E-05	2.7E-05
	90	1.4E-04	1.4E-04	1.3E-04	1.2E-04	1.1E-04	9.6E-05	7.2E-05	5.6E-05	5.1E-05	4.6E-05
Bakersfield	50	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	60	1.7E-05	1.3E-05	9.8E-06	4.9E-06	2.1E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	5.8E-05	5.4E-05	4.9E-05	4.1E-05	3.4E-05	2.2E-05	9.8E-06	2.1E-06	7.0E-07	7.0E-07
	75	7.7E-05	7.4E-05	6.8E-05	6.0E-05	5.1E-05	3.9E-05	2.2E-05	1.3E-05	9.8E-06	5.6E-06
	80	9.6E-05	9.4E-05	8.9E-05	7.9E-05	7.1E-05	5.6E-05	3.7E-05	2.4E-05	1.9E-05	1.5E-05
	85	1.2E-04	1.2E-04	1.1E-04	1.0E-04	9.1E-05	7.6E-05	5.3E-05	3.9E-05	3.2E-05	2.9E-05
	90	1.5E-04	1.4E-04	1.4E-04	1.3E-04	1.2E-04	1.0E-04	7.3E-05	5.6E-05	4.9E-05	4.4E-05
Bradenton	50	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	60	9.8E-06	7.0E-06	3.5E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	5.8E-05	5.1E-05	4.4E-05	3.2E-05	2.2E-05	1.2E-05	2.1E-06	7.0E-07	7.0E-07	7.0E-07
	75	8.5E-05	7.9E-05	7.1E-05	5.9E-05	4.8E-05	3.2E-05	1.4E-05	5.6E-06	3.5E-06	2.1E-06
	80	1.1E-04	1.1E-04	9.9E-05	8.6E-05	7.6E-05	5.6E-05	3.4E-05	2.0E-05	1.5E-05	1.2E-05
	85	1.4E-04	1.3E-04	1.3E-04	1.1E-04	1.0E-04	8.3E-05	5.6E-05	3.9E-05	3.4E-05	2.9E-05
	90	1.7E-04	1.7E-04	1.6E-04	1.5E-04	1.3E-04	1.1E-04	8.1E-05	6.2E-05	5.4E-05	4.8E-05
Flint	50	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	--	--	--
	60	1.3E-05	9.8E-06	7.0E-06	3.5E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	4.6E-05	4.4E-05	3.9E-05	3.1E-05	2.4E-05	1.4E-05	4.9E-06	7.0E-07	7.0E-07	7.0E-07
	75	6.3E-05	6.0E-05	5.6E-05	4.9E-05	4.2E-05	2.9E-05	1.5E-05	7.7E-06	5.6E-06	3.5E-06
	80	7.8E-05	7.6E-05	7.2E-05	6.5E-05	5.9E-05	4.6E-05	2.9E-05	2.0E-05	1.7E-05	1.3E-05
	85	9.4E-05	9.1E-05	8.8E-05	8.0E-05	7.4E-05	6.2E-05	4.4E-05	3.4E-05	2.9E-05	2.5E-05
	90	1.1E-04	1.1E-04	1.1E-04	1.0E-04	9.4E-05	7.9E-05	6.0E-05	4.6E-05	4.2E-05	3.9E-05
Tallahassee	50	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	60	1.1E-05	7.7E-06	4.9E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	5.1E-05	4.6E-05	3.9E-05	3.1E-05	2.2E-05	1.2E-05	2.1E-06	7.0E-07	7.0E-07	7.0E-07
	75	7.1E-05	6.6E-05	6.1E-05	5.1E-05	4.4E-05	3.1E-05	1.4E-05	5.6E-06	3.5E-06	2.1E-06
	80	9.0E-05	8.6E-05	8.0E-05	7.2E-05	6.3E-05	5.1E-05	3.1E-05	2.0E-05	1.5E-05	1.3E-05
	85	1.1E-04	1.1E-04	1.0E-04	9.3E-05	8.5E-05	7.1E-05	5.1E-05	3.7E-05	3.2E-05	2.7E-05
	90	1.3E-04	1.3E-04	1.3E-04	1.2E-04	1.1E-04	9.5E-05	7.1E-05	5.5E-05	4.9E-05	4.4E-05
Yakima	50	1.3E-05	9.8E-06	7.0E-06	3.5E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	60	3.9E-05	3.4E-05	2.9E-05	2.2E-05	1.5E-05	7.7E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	6.1E-05	5.8E-05	5.3E-05	4.4E-05	3.7E-05	2.7E-05	1.5E-05	7.7E-06	5.6E-06	3.5E-06
	75	7.3E-05	6.9E-05	6.5E-05	5.6E-05	4.9E-05	3.9E-05	2.4E-05	1.5E-05	1.3E-05	1.1E-05
	80	8.6E-05	8.3E-05	7.8E-05	6.9E-05	6.1E-05	5.1E-05	3.4E-05	2.5E-05	2.2E-05	1.8E-05
	85	1.0E-04	9.9E-05	9.4E-05	8.5E-05	7.7E-05	6.3E-05	4.6E-05	3.4E-05	3.1E-05	2.7E-05
	90	1.2E-04	1.2E-04	1.2E-04	1.1E-04	9.6E-05	8.1E-05	6.1E-05	4.8E-05	4.4E-05	3.9E-05

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.
Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\ -1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(8 application days/365-day year) x (50 years exposed/78-yr lifetime).
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.9. Cancer Risk Estimates for Varied Distances from a 10-Acre Treated Field - Ornamentals[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	60	3.4E-05	2.9E-05	2.2E-05	1.3E-05	7.0E-06	2.1E-06	7.0E-07	7.0E-07	7.0E-07	7.0E-07
	70	7.9E-05	7.4E-05	6.6E-05	5.5E-05	4.6E-05	3.1E-05	1.3E-05	4.9E-06	2.1E-06	7.0E-07
	75	9.9E-05	9.5E-05	8.8E-05	7.7E-05	6.6E-05	5.1E-05	2.9E-05	1.8E-05	1.3E-05	9.8E-06
	80	1.2E-04	1.1E-04	1.1E-04	9.7E-05	8.8E-05	7.2E-05	4.9E-05	3.4E-05	2.9E-05	2.4E-05
	85	1.4E-04	1.4E-04	1.3E-04	1.2E-04	1.1E-04	9.5E-05	7.1E-05	5.5E-05	4.9E-05	4.4E-05
	90	1.8E-04	1.8E-04	1.7E-04	1.6E-04	1.5E-04	1.3E-04	1.0E-04	8.0E-05	7.3E-05	6.7E-05
Bakersfield	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	60	2.4E-05	2.2E-05	1.8E-05	1.2E-05	7.9E-06	2.6E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	5.8E-05	5.6E-05	5.1E-05	4.5E-05	3.8E-05	2.9E-05	1.6E-05	8.9E-06	5.8E-06	4.2E-06
	75	7.5E-05	7.2E-05	6.7E-05	6.0E-05	5.4E-05	4.3E-05	2.8E-05	1.9E-05	1.5E-05	1.3E-05
	80	9.2E-05	8.9E-05	8.5E-05	7.7E-05	7.1E-05	5.8E-05	4.2E-05	2.9E-05	2.6E-05	2.2E-05
	85	1.1E-04	1.1E-04	1.1E-04	9.7E-05	8.9E-05	7.6E-05	5.6E-05	4.3E-05	3.8E-05	3.3E-05
	90	1.4E-04	1.3E-04	1.3E-04	1.2E-04	1.1E-04	9.7E-05	7.6E-05	5.9E-05	5.4E-05	4.8E-05
Bradenton	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	60	1.7E-05	1.3E-05	8.9E-06	4.2E-06	2.6E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	6.1E-05	5.7E-05	4.9E-05	4.1E-05	3.3E-05	2.1E-05	7.9E-06	2.6E-06	1.6E-06	5.3E-07
	75	8.4E-05	7.9E-05	7.2E-05	6.2E-05	5.4E-05	4.1E-05	2.3E-05	1.3E-05	9.5E-06	7.4E-06
	80	1.1E-04	1.0E-04	9.6E-05	8.5E-05	7.6E-05	6.2E-05	4.2E-05	2.9E-05	2.4E-05	2.0E-05
	85	1.3E-04	1.3E-04	1.2E-04	1.1E-04	1.0E-04	8.4E-05	6.1E-05	4.6E-05	4.1E-05	3.6E-05
	90	1.6E-04	1.5E-04	1.5E-04	1.4E-04	1.3E-04	1.1E-04	8.3E-05	6.6E-05	5.9E-05	5.4E-05
Flint	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	0.0E+00
	60	1.9E-05	1.6E-05	1.3E-05	7.9E-06	4.2E-06	1.6E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	4.8E-05	4.6E-05	4.2E-05	3.6E-05	3.1E-05	2.2E-05	1.1E-05	4.2E-06	2.6E-06	1.6E-06
	75	6.2E-05	5.9E-05	5.6E-05	5.1E-05	4.5E-05	3.5E-05	2.2E-05	1.4E-05	1.2E-05	8.9E-06
	80	7.4E-05	7.2E-05	6.9E-05	6.4E-05	5.8E-05	4.8E-05	3.5E-05	2.6E-05	2.2E-05	1.9E-05
	85	8.8E-05	8.7E-05	8.3E-05	7.7E-05	7.2E-05	6.2E-05	4.7E-05	3.8E-05	3.3E-05	2.9E-05
	90	1.1E-04	1.1E-04	1.0E-04	9.6E-05	8.9E-05	7.8E-05	6.1E-05	4.9E-05	4.5E-05	4.2E-05
Tallahassee	50	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	60	1.8E-05	1.4E-05	9.5E-06	5.3E-06	2.6E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	70	5.3E-05	4.9E-05	4.5E-05	3.7E-05	3.1E-05	2.1E-05	7.9E-06	2.6E-06	1.6E-06	5.3E-07
	75	6.9E-05	6.7E-05	6.2E-05	5.5E-05	4.7E-05	3.7E-05	2.2E-05	1.3E-05	9.5E-06	7.4E-06
	80	8.5E-05	8.4E-05	7.9E-05	7.2E-05	6.5E-05	5.4E-05	3.8E-05	2.7E-05	2.3E-05	2.0E-05
	85	1.0E-04	1.0E-04	9.7E-05	9.0E-05	8.3E-05	7.2E-05	5.4E-05	4.2E-05	3.8E-05	3.4E-05
	90	1.3E-04	1.2E-04	1.2E-04	1.1E-04	1.1E-04	9.4E-05	7.4E-05	5.9E-05	5.4E-05	5.1E-05
Yakima	50	1.8E-05	1.5E-05	1.2E-05	7.4E-06	3.7E-06	5.3E-07	5.3E-07	5.3E-07	5.3E-07	5.3E-07
	60	3.8E-05	3.6E-05	3.2E-05	2.5E-05	2.1E-05	1.3E-05	5.3E-06	1.6E-06	5.3E-07	5.3E-07
	70	5.8E-05	5.6E-05	5.1E-05	4.5E-05	3.9E-05	3.1E-05	2.0E-05	1.3E-05	1.1E-05	7.9E-06
	75	6.9E-05	6.7E-05	6.3E-05	5.6E-05	4.9E-05	4.1E-05	2.8E-05	2.0E-05	1.7E-05	1.5E-05
	80	8.2E-05	7.8E-05	7.4E-05	6.7E-05	6.1E-05	5.1E-05	3.8E-05	2.9E-05	2.5E-05	2.2E-05
	85	9.6E-05	9.3E-05	8.8E-05	8.1E-05	7.5E-05	6.4E-05	4.8E-05	3.8E-05	3.5E-05	3.2E-05
	90	1.2E-04	1.1E-04	1.1E-04	1.0E-04	9.4E-05	8.1E-05	6.3E-05	5.1E-05	4.7E-05	4.2E-05

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.
Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\ -1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(8 application days/365-day year) x (50 years exposed/78-yr lifetime).
Highlighted column indicates buffer zone proposed on label for this use.

Table 5.2.10. Cancer Risk Estimates for Varied Distances from a 40-Acre Treated Field – Bare Soil[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	6.8E-07	6.8E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07
	75	1.6E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07
	80	1.6E-06	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	6.8E-07	4.6E-07	4.6E-07	4.6E-07
	85	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07
	90	1.8E-06	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	1.0E-06	6.8E-07
Bakersfield	50	4.6E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	1.0E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	4.6E-07	4.6E-07	4.6E-07
	75	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07
	80	2.2E-06	2.2E-06	1.8E-06	1.8E-06	1.6E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07
	85	2.4E-06	2.4E-06	2.2E-06	2.2E-06	1.8E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07
	90	2.7E-06	2.7E-06	2.4E-06	2.4E-06	2.2E-06	1.8E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06
Bradenton	50	4.6E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	1.0E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	4.6E-07	4.6E-07	4.6E-07
	75	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07
	80	2.2E-06	2.2E-06	1.8E-06	1.8E-06	1.6E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07
	85	2.4E-06	2.4E-06	2.2E-06	2.2E-06	1.8E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07
	90	2.7E-06	2.7E-06	2.4E-06	2.4E-06	2.2E-06	1.8E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06
Flint	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	6.8E-07	6.8E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.0E-06	1.0E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07
	75	1.3E-06	1.3E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	4.6E-07	4.6E-07	4.6E-07
	80	1.6E-06	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07	4.6E-07
	85	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07
	90	2.2E-06	2.2E-06	1.8E-06	1.8E-06	1.8E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	1.0E-06
Tallahassee	50	4.6E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	6.8E-07	6.8E-07	6.8E-07	6.8E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07
	75	1.3E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07	4.6E-07
	80	1.6E-06	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07
	85	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.6E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07
	90	2.2E-06	2.2E-06	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07
Yakima	50	6.8E-07	6.8E-07	6.8E-07	4.6E-07	4.6E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	1.0E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07	4.6E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.3E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07	4.6E-07
	75	1.6E-06	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	4.6E-07	4.6E-07
	80	1.8E-06	1.8E-06	1.6E-06	1.6E-06	1.3E-06	1.3E-06	1.0E-06	6.8E-07	6.8E-07	6.8E-07
	85	2.2E-06	2.2E-06	1.8E-06	1.8E-06	1.6E-06	1.3E-06	1.0E-06	1.0E-06	6.8E-07	6.8E-07
	90	2.4E-06	2.4E-06	2.4E-06	2.2E-06	1.8E-06	1.8E-06	1.3E-06	1.3E-06	1.0E-06	1.0E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Florida tomato farm (bare soil) Field 1 flux profile, with an application rate of 390 lb ai/A. Values presented reflect the total air concentration (i.e., furfural plus furfuryl alcohol) as furfuryl alcohol was found to occur as a soil degradate (up to 30% of parent) when furfural is applied to bare ground.
Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\,-1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(1 application day/365-day year) x (50 years exposed/78-yr lifetime).
Highlighted column indicates buffer zone proposed on label for this use.

6. CUMULATIVE RISK

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to furfural and any other substances, and furfural does not appear to produce a toxic metabolite produced by other substances. For the purposes of this registration action, therefore, EPA has not assumed that furfural has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

7. OCCUPATIONAL EXPOSURE

The end-use product containing 90% furfural in a liquid formulation (MULTIGUARD PROTECT® EC) is proposed for use on bare soil as a pre-plant treatment for fruiting vegetables, curcurbits, citrus, pome fruit, stone fruit, berries and tree nuts. It is also currently registered on athletic fields, golf courses (tees, greens, and spot treatment of fairways and roughs), sod farms and outdoor ornamentals, for which exposure is being reevaluated based on the cancer reclassification. Applications may be made via shank injection, chemigation, groundboom sprayer, and mechanically-pressurized handgun. There is potential for dermal and inhalation exposure during handling and post-application activities.

7.1. Occupational Handler Exposures and Risks

There is a potential for short- and intermediate-term exposure to furfural during mixing, loading, and application activities. Chronic exposure is not expected for the proposed use patterns associated with furfural. No chemical-specific handler exposure data were submitted in support of this registration. It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include the PHED 1.1, the AHETF database, the ORETF database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (http://www.epa.gov/opp00001/science/handler-exposure-table.pdf), which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at http://www.epa.gov/pesticides/science/handler-exposure-data.html.

Exposure assumptions and MOEs for occupational handlers are summarized in Table 7.1. The results of the handler occupational exposure and risk assessment indicate that dermal non-cancer risk estimates are not of concern (i.e., MOEs greater than the LOC of 100) when gloves are worn for mixing/loading. The dermal MOEs range from 33 (190 with gloves) to 1,400. Inhalation MOEs range from 270 to 5,700 without a respirator, and therefore, are not of concern. The

proposed label requires chemical-resistant gloves for all handlers and the addition of coveralls when using handheld equipment.

The results of the cancer assessment for handlers for private growers/owners and commercial operations are summarized in Tables 7.2 and 7.3, respectively. For private growers/owners, the cancer risk estimates at the maximum levels of mitigation (gloves, coveralls and a respirator, or engineering controls) range from 9E-6 to 5E-5. These risk estimates represent those of a private owner/grower, assuming 10 days of exposure per year; this does not account for commercial applicators completing multiple applications for multiple clients. The standard assumption for commercial applicators is 30 days, for which cancer risks range from 3E-5 to 2E-4. Occupational cancer risks are estimated using standard amortization factors including an assumed 35 years of exposure out of a 78-year lifetime. As discussed previously, the Registration Division requested additional occupational handler cancer risk estimates based on time-limited exposure durations of 10 years for currently registered uses and 5 years for the proposed use; these cancer risk estimates are provided in Appendix G.

The minimum level of PPE for handlers is based on acute toxicity for the end-use products. The Registration Division (RD) is responsible for ensuring that PPE listed on the label is in compliance with the Worker Protection Standard (WPS).

Table 7.1. Summary of MOEs for Occupational Handlers of Furfural							
Exposure Scenario (Scenario #)	**Exposure Route**	**Unit Exposure (µg/lb ai) [1]**	**Use Site**	**Application Rate (lb ai/A)[2]**	**Area Treated (A/day) [3]**	**Dose (mg/kg/day) [4]**	**Short- and Int-term MOE [5]**
Mixer/Loader							
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves)	Bare Soil	69.5	40	7.65 1.31 (gloves)	**33** 190 (gloves)
	Inhalation	0.219				0.0076	270
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves)	Bare Soil	69.5	40	7.65 1.31 (gloves)	**33** 190 (gloves)
	Inhalation	0.219				0.0076	270
	Dermal	220	Ornamentals	47.7	10	1.3	190
	Inhalation	0.219				0.0013	1,600
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220	Golf course, Athletic Fields & Sod Farms	69.5	10	1.91	130
	Inhalation	0.219				0.0019	1,100
Applicator							
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6	Golf course, Athletic Fields & Sod Farms	69.5	10	0.683	370
	Inhalation	0.34				0.00295	710
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	0.18	1,400
	Inhalation	0.043 (closed cab)				0.0015	1,400
Mixer/Loader/Applicator							
(6) Mixing/Loading Liquid	Dermal	6,050		0.0034	1,000	0.26	970

Table 7.1. Summary of MOEs for Occupational Handlers of Furfural

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Dose (mg/kg/day) [4]	Short- and Int-term MOE [5]
and Applying with Mechanically-pressurized Handgun Sprayer	Inhalation	8.68	Ornamentals (soil drench)	(lb ai/gal)	(gal/day)	0.00037	5,700

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Daily Dose (mg/kg/day) = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated) / Body Weight (80 kg)

[5] Short-/Intermediate-Term MOE = NOAEL / Daily Dose. The dermal NOAEL = 250 mg/kg/day, and the inhalation NOAEL = 2.09 mg/kg/day [Note: the dose in mg/L was converted to mg/kg/day using the following equation: Dose (mg/kg/day) = (NOAEL (0.008 mg/L) * Respiration rate of a young adult Sprague-Dawley rat (10.26 L/hr) * Study daily exposure duration (6 hr/day)) / Body weight of a young adult Sprague-Dawley rat (0.236 kg)]. The LOC is 100 for inhalation as well as dermal exposure because the RfC methodology was not employed in these calculations.

Table 7.2. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – Private Owner/Grower

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Mixer/Loader								
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves) 29.1 (gloves + DL) 8.6 (closed system)	Bare Soil	69.5	40	10	0.0094 0.0016 (gloves) 0.0012 (gloves + DL) 0.00037 (closed system)	**1E-3** **2E-4 (gloves)** **2E-4 (gloves + DL)** **2E-4 (G/DL + resp)** **5E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000094 0.0000094 (resp) 0.000036 (closed system)	
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Bare Soil	69.5	40	10	0.0094 0.0016 (gloves) 0.0012 (gloves + DL) 0.00037 (closed system)	**1E-3** **2E-4 (gloves)** **2E-4 (gloves + DL)** **2E-4 (G/DL + resp)** **5E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000094 0.0000094 (resp) 0.000036 (closed system)	
	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Ornamentals	47.7	10	10	0.0016 0.00028 (gloves) 0.00021 (gloves + DL) 0.000063 (closed system)	**2E-4** **4E-5 (gloves)** **3E-5 (gloves + DL)** **3E-5 (G/DL + resp)** **9E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000016 0.0000016 (resp) 0.0000061 (closed system)	
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	10	0.0024 0.00040 (gloves) 0.00031 (gloves + DL) 0.000092 (closed system)	**3E-4** **6E-5 (gloves)** **4E-5 (gloves + DL)** **4E-5 (G/DL + resp)** **1E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000023 0.0000023 (resp) 0.0000089 (closed system)	

Table 7.2. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – Private Owner/Grower

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Applicator								
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6 16.1 (gloves) 12.6 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	10	0.00084 0.00017 (gloves) 0.00014 (gloves + DL)	**1E-4** **3E-5 (gloves)** **2E-5 (gloves + DL)** **2E-5 (G/DL + resp)**
	Inhalation	0.34 0.034 (resp)					0.000036 0.0000036 (resp)	
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	10	0.00022	**3E-5**
	Inhalation	0.043 (closed cab)					0.000018	
Mixer/Loader/Applicator								
(8) Mixing/Loading Liquid and Applying with Mechanically-pressurized Handgun Sprayer	Dermal	6,050 2,050 (gloves) 1,360 (gloves+DL)	Ornamentals (soil drench)	0.0034 (lb ai/gal)	1,000 (gal/day)	10	0.00032 0.00011 (gloves) 0.000071 (gloves + DL)	**4E-5** **1E-5 (gloves)** **1E-5 (gloves + DL)** **9E-6 (G/DL + resp)**
	Inhalation	8.68 0.87 (resp)					0.0000045 0.00000045 (resp)	

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Days Exposed/Treatments per year is based on a standard assumption for a private owner/grower. Note, the assumption of 10 days per year does not account for commercial applicators completing multiple applications for multiple clients; for estimates regarding commercial applicators (30 days exposure) – See Table 7.3.

[5] LADD (mg/kg/day) = Daily Dose (mg/kg/day) × [Days exposed/treatments per year (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (35 yrs) ÷ Lifetime expectancy (yrs)]; where Daily Dose = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated * Absorption factor (10% for dermal; 100% for inhalation) / Body Weight (80 kg)

[6] Cancer risk estimates = Total LADD [Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day)] × Q_1^*, where Q_1^* = **0.131** $(mg/kg/day)^{-1}$

Table 7.3. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – Commercial Operations

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Mixer/Loader								
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves) 29.1 (gloves + DL) 8.6 (closed system)	Bare Soil	69.5	40	30	0.0094 0.0016 (gloves) 0.0012 (gloves + DL) 0.00037 (closed system)	**3E-3** **6E-4 (gloves)** **6E-4 (gloves + DL)** **6E-4 (G/DL + resp)** **2E-4 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000094 0.0000094 (resp) 0.000036 (closed system)	
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Bare Soil	69.5	40	30	0.0094 0.0016 (gloves) 0.0012 (gloves + DL) 0.00037 (closed system)	**3E-3** **6E-4 (gloves)** **6E-4 (gloves + DL)** **6E-4 (G/DL + resp)** **2E-4 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000094 0.0000094 (resp) 0.000036 (closed system)	
	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Ornamentals	47.7	10	30	0.0016 0.00028 (gloves) 0.00021 (gloves + DL) 0.000063 (closed system)	**6E-4** **1E-4 (gloves)** **9E-5 (gloves + DL)** **9E-5 (G/DL + resp)** **3E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000016 0.0000016 (resp) 0.0000061 (closed system)	
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	30	0.0024 0.00040 (gloves) 0.00031 (gloves + DL) 0.000092 (closed system)	**9E-4** **2E-4 (gloves)** **1E-4 (gloves + DL)** **1E-4 (G/DL + resp)** **3E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000023 0.0000023 (resp) 0.0000089 (closed system)	

Table 7.3. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – Commercial Operations

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Applicator								
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6 16.1 (gloves) 12.6 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	30	0.00084 0.00017 (gloves) 0.00014 (gloves + DL)	**3E-4** **9E-5 (gloves)** **6E-5 (gloves + DL)** **6E-5 (G/DL + resp)**
	Inhalation	0.34 0.034 (resp)					0.000036 0.0000036 (resp)	
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	30	0.00022	**9E-5**
	Inhalation	0.043 (closed cab)					0.000018	
Mixer/Loader/Applicator								
(8) Mixing/Loading Liquid and Applying with Mechanically-pressurized Handgun Sprayer	Dermal	6,050 2,050 (gloves) 1,360 (gloves+DL)	Ornamentals (soil drench)	0.0034 (lb ai/gal)	1,000 (gal/day)	30	0.00032 0.00011 (gloves) 0.000071 (gloves + DL)	**1E-4** **3E-5 (gloves)** **3E-5 (gloves + DL)** **3E-5 (G/DL + resp)**
	Inhalation	8.68 0.87 (resp)					0.0000045 0.00000045 (resp)	

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Days Exposed/Treatments per year is based on a standard assumption for commercial applicators completing multiple applications for multiple clients; 30 days.

[5] LADD (mg/kg/day) = Daily Dose (mg/kg/day) × [Days exposed/treatments per year (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (35 yrs) ÷ Lifetime expectancy (yrs)]; where Daily Dose = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated * Absorption factor (10% for dermal; 100% for inhalation) / Body Weight (80 kg)

[6] Cancer risk estimates = Total LADD [Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day)] × Q_1^*, where Q_1^* = **0.131** $(mg/kg/day)^{-1}$

7.2. Occupational Post-application Exposures and Risks

This registration action for furfural involves application to bare soil as a pre-plant treatment for fruiting vegetables, curcurbits, citrus, pome fruit, stone fruit, berries and tree nuts. It also incorporates a reevaluation of exposure associated with the currently registered uses on athletic fields, golf courses (tees, greens, and spot treatment of fairways and roughs), sod farms and outdoor ornamentals, based on the cancer reclassification. Post-application inhalation exposure to furfural is expected to be likely (vapor pressure = 2.6 mmHg).

As discussed previously, although the currently registered uses indicate a potential for post-application contact with furfural residues on treated fields/golf courses and ornamentals, DFR/TTR decreased to negligible levels within 4 hours of application (i.e., 0.00297 µg/cm^2 compared to the LOQ of 0.00135 µg/cm^2). Therefore, exposure via these scenarios is expected to be negligible, and a quantitative dermal assessment was not conducted.

Inhalation post-application exposure

Identical to the bystander assessment, buffer zones were estimated for 6 meteorological regions for several field sizes ranging from one acre to 40 acres. The range in field sizes is provided to bracket the proposed and currently registered use patterns. For golf courses the label indicates that spot treatment is limited to not more than one contiguous acre. Athletic fields were assumed to be within sports complexes estimated to be 3 acres; this was also assumed to be the treated area for sod farms (reduced on the proposed label to spot treatment only, up to 3 contiguous acres). The proposed label limits field-grown ornamental and bare soil treatments to maximum areas of 10 and 40 acres, respectively, in a 24-hour period.

Although it possible for workers near the treated field to be exposed to emissions for the full workday, a 6-hour averaging time was used to calculate the air concentrations for workers because flux measurements dropped to negligible levels within this period. This timeframe also matches the duration of the acute inhalation toxicity study on which the COC is based.

The flux profile from Field 3 in the Florida turf study was used in calculating the emissions for treated golf courses, athletic fields, sod farms and ornamentals. The analysis was limited to this flux profile because it is the most representative of the potential emissions from these use sites, based on the revised label application instructions (i.e., specification of a maximum spray release height of two feet above the ground with a coarse spray setting or in-ground irrigation systems).

To estimate the emissions for pre-plant bare soil treatments, the Field 1 flux profile from the Florida tomato farm (bare soil) study was used. Although this study also measured air concentrations of furfuryl alcohol, a soil degradate of furfural, the recovery data were unacceptable; therefore a surrogate method of estimating furfuryl alcohol air concentrations was employed by extrapolating the ratio of furfuryl alcohol to furfural detected in the soil samples

(up to 30% of parent), and adjusting the furfural air concentration to reflect the additional contribution of furfuryl alcohol. Because the toxicity endpoints for furfural are considered to be relevant for furfuryl alcohol, the adjusted concentration was compared to the COC and Q*.

The bystander inhalation assessment (summarized previously in Section 5.2) is protective of occupational post-application inhalation exposure. Tables 5.2.1 through 5.2.5 present MOEs based on the whole field distribution. The 75th percentile MOEs for the various field sizes range from 27 to 232 at the label-proposed buffer zones (5 to 15 meters); the LOC is for MOEs less than 30. The corresponding cancer risk estimates, which are presented in Tables 5.2.6 through 5.2.10 range from 1.3E-6 to 8.5E-5. These cancer risks are estimated using standard amortization factors including an assumed 50 years of exposure out of a 78-year lifetime. As discussed previously, the Registration Division requested additional cancer risk estimates based on time-limited exposure durations of 10 years for currently registered uses and 5 years for the proposed use; these cancer risk estimates are provided in Appendix F.

As indicated previously, the predicted air concentrations at varied distances from treated fields that range from one to 40 acres in size are provided in Appendix E. Tables E1 through E4 are based on the Field 3 flux profile (from the turf study), and Table E5 is based on the Field 1 flux profile from the tomato farm bare soil study.

Dermal post-application exposure

The results of the DFR study (discussed previously) indicate that furfural residues decline to negligible levels within 4 hours of application. Therefore, occupational post-application exposure to furfural residues on treated turf is expected to be negligible, and a quantitative assessment was not conducted. The furfural technical material has been classified in Toxicity Category III for acute dermal toxicity (reclassification D383688, B. Hanson, 12/16/10), Category IV for acute dermal irritation, and Category II for primary eye irritation. Per the Worker Protection Standard (WPS), a 24-hr restricted entry interval (REI) is required for chemicals classified under Toxicity Category II and a 12-hr REI is required for chemicals classified under Toxicity Category III and IV. The proposed furfural label indicates an REI of 12 hours, which is adequate given the results of the DFR study. This product is proposed for use on bare ground as a pre-plant application for agricultural crops, and is registered for use on outdoor ornamentals, sod and seed farms, which are within the scope of the WPS, therefore, the REI on the label is appropriate. Furfural is also registered for use on athletic fields and golf courses, to which the WPS does not apply; the label correctly contains language cautioning unprotected persons to keep out of treated areas until sprays have dried.

8. DATA NEEDS/LABEL REQUIREMENTS

8.1 Chemistry

- None

8.2 Toxicology

- None
- [Note: Mode of action studies are currently being developed by the registrant for the tumor types seen in animals treated with furfural or furfuryl alcohol.]

8.3 Exposure

Data requirements:

- none

Label change recommendations:

- Include a statement indicating a closed system for mixing/loading for bare soil application (based on cancer risk estimates).
- Include a statement indicating that for mixing/loading for all other application methods, as well as mixing/loading/applying for handheld applications, handlers must wear chemical-resistant gloves and coveralls (based on cancer risk estimates).
- Proposed buffer zones: ensure proper distance relative to area treated for all charts (e.g., for ornamentals, the buffer zone distance should be at least 45 feet [i.e., 15 meters] for treatment areas of 3 to 10 acres, which is consistent with a sod farm treatment area of 3 acres having a proposed buffer zone of 45 feet).

Data compensation:

- Data from the Outdoor Residential Exposure Task Force (ORETF) and Agricultural Re-entry Task Force (ARTF) were used in this assessment. Data compensation considerations apply.

APPENDIX A: Executive Summaries and Toxicological Profile

A.1 Toxicology Data Requirements

The requirements (40 CFR 158.340) for non-food use for Furfural are shown below in Table A1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Table A1. Toxicology Data Requirements

Test		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	CR	yes
870.3150	Oral Subchronic (nonrodent)	CR	--
870.3200	21/28-Day Dermal	CR	yes
870.3250	90-Day Dermal	CR	yes[1]
870.3465	90-Day Inhalation	CR	yes[2]
870.3700a	Developmental Toxicity (rodent)	CR	yes
870.3700b	Developmental Toxicity (nonrodent)	CR	yes
870.3800	Reproduction	CR	yes
870.4100a	Chronic Toxicity (rodent)	CR	yes
870.4100b	Chronic Toxicity (nonrodent)	CR	--
870.4200a	Oncogenicity (rat)	CR	yes
870.4200b	Oncogenicity (mouse)	CR	yes
870.4300	Chronic/Oncogenicity	CR	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5375	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5550	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a	Acute Delayed Neurotox. (hen)	CR	--
870.6100b	90-Day Neurotoxicity (hen)	CR	--
870.6200a	Acute Neurotox. Screening Battery (rat)	CR	yes
870.6200b	90-Day Neuro. Screening Battery (rat)	CR	waived[3]
870.6300	Develop. Neuro	--	--
870.7485	General Metabolism	CR	yes
870.7600	Dermal Penetration	CR	no
870.7800	Immunotoxicity	CR	yes

CR: conditionally required;
[1]The 28-day dermal toxicity study (870.3200) in rats fulfills the 870.3250 Guideline for 90-day dermal toxicity study in rats.
[2] The 28-day inhalation toxicity study in rats fulfills the 870.3465 Guideline for 90-day inhalation toxicity study
[3]Waived by HASPOC (TXR No. 0056939;D418688;6/10/2014)

A.2 Toxicity Profiles

Table A.2.1 Acute Toxicity Profile - Furfural				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute oral in rats (Rana, 2002)	46011009	LD_{50} = >102 mg/kg	II
870.1200	Acute dermal in rats (Moore, 2004)	46406102	LD_{50} > 2,000 mg/kg	III*****
870.1300	Acute inhalation in rats. (Merkel, 2003)	46106302	LC_{50} = 0.54-1.63 mg/L	III
870.2400	Acute eye irritation in rabbits. (Joseph, 2003)	46011012	Severe. Irritant.	II
870.2500	Acute dermal irritation in rabbits. (Joseph, 2003)	46011013	Slight. Irritant.	IV
870.2600	Skin sensitization in Guinea pigs. (Joseph, 2003)	46011014	Non sensitizer.	Neg.

***** There have been several Acute Dermal LD_{50} studies submitted in support of furfural:

Joseph, S. A. (2003). Acute Dermal Toxicity Study of Furfural in Rats. Jai Research Foundation, Department of Toxicology, Valvada, Valsad, Gujrat, India. Study No. 3950 dated 5-23-03. MRID 46011010 – **Toxicity Category I**

Mukherjee, A. (2003) Acute Dermal Toxicity Study of MultiguardTM Protect in Rats. Jai Research Foundation, Dept. of Toxicology, Valvada - 396108, Dist. Valsad, Gujarat, India. JRF Study No. 4228. Study Completion Date: 12 May 2003. MRID 46028102. Unpublished – **Toxicity Category I**

Moore, G. (2004) Acute Dermal Toxicity Study in Rats. Laboratory Study No.: 15621. Unpublished study prepared by Product Safety Laboratories. September 27, 2004. MRID 46406102 – **Toxicity Category III**

Moore, G. (2004) Acute Dermal Toxicity Study in Rats - Defined LD50. Laboratory Study No.: 15139. Unpublished study prepared by Product Safety Laboratories. September 27, 2004. MRID 46406103 – **Toxicity Category III**

Moore, G. (2004) Acute Dermal Toxicity Study in Rats - Defined LD50. Laboratory Study No.: 16080. Unpublished study prepared by Product Safety Laboratories. November 18, 2004. MRID 46424101 – **Toxicity Category III**

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile for Furfural		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Non-guideline Acute inhalation with complete recovery	48563701 (2011) Acceptable/**Non-guideline** 0, 10, 20, 40 mg/m^3 for 6 hours. Satellite group with 14 day recovery period	LOAEL = Not observed NOAEL = 40 mg/m^3
870.3100 90-Day oral toxicity rats	46011015 (1990) Acceptable/**Non-guideline** 0, 11, 22, 45, 90, 180 mg/kg/day (gavage in corn oil)	NTP 1990 Study **(publication).** Systemic Toxicity NOAEL = 45 mg/kg/day Systemic Toxicity LOAEL = 90 mg/kg/day based on liver pathology – cytoplasmic vacuolization of hepatocytes. **Limited parameters measured.**
870.3100 90-Day oral toxicity mice.	46011015 (1990) Acceptable/ **Non-guideline** 0, 75, 150, 300, 600, 1200 mg/kg/day (gavage in corn oil)	NTP 1990 Study (**publication**). Systemic Toxicity NOAEL= not observed Systemic Toxicity LOAEL = 75 mg/kg/day based on relative liver weights. **Limited parameters measured.**
870.3100 90-Day oral toxicity rats.	46011015 (2001) Summary/**Non-guideline (WHO published review article)** 0, 30, 60, 90, 180 mg/kg/day (microencapsulated and mixed into feed)	WHO **(published review article),** Food Additive Series 46 (2001) Systemic Toxicity NOAEL = 60 mg/kg/day Systemic Toxicity LOAEL = 90 mg/kg/day based on liver effects.
870.3200 28-Day dermal toxicity in rats.	46465501 (2004) Unacceptable/**Guideline** 0, 25, 50 and 100 mg/kg	Systemic Toxicity NOAEL = 100 mg/kg/day (HDT). Systemic Toxicity LOAEL was not observed. No dermal irritation noted.
870.3200 28-Day dermal toxicity in rats.	46917201and 46917202 (2006) Acceptable/**Guideline** 0, 100, 250, 500, or 1000 mg/kg bw/day, 6 hours/day for 5 days/week	Systemic Toxicity NOAEL = 250 mg/kg/day Systemic Toxicity LOAEL = 500 mg/kg/day based on adverse clinical signs (males), an increase in motor activity (males) and increased mortality (males and females). No dermal irritation noted.
870.3250 90-Day dermal toxicity in rats		28-day dermal toxicity study fulfills this requirement
870.6200a Acute Neurotoxicity - rat	48998502 (main) (2012) Acceptable/Guideline 0, 30, 80, 200 mg/kg [48998501 (range finding) (2012) 0, 50, 100, 150 mg/kg]	NOAEL = 80 mg/kg LOAEL = 200 mg/kg based on mortality and effects on FOB parameters and motor activity in males and females

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile for Furfural		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.6200b Subchronic Neurotoxicity - rat		**Waived by HASPOC (TXR No. 0056939; D418688;6/10/2014)**
870.3465 28-Day inhalation toxicity in rats	46426504 and 46426505(2001) Acceptable/Guideline 0, 20, 40, 80, 160, 320, 640, 1280 mg/m^3	NTO (Netherlands) 2001 (**study publication**). Systemic Toxicity NOAEL < 20 mg/m^3. Systemic Toxicity LOAEL = < 20 mg/m^3. (LDT) all dose levels showing nasal epithelium pathology.
870.3465 28-Day inhalation toxicity in rats	47419101 (2008) Acceptable/Guideline 0 (air), 2, 4, 8, or 20 mg/m^3 (equivalent to analytical concentrations of 0, 0.002, 0.004, 0.007, and 0.017 mg/L, respectively) for 6 hours per day, 5 days/week for 4 weeks	**Portal of Entry** NOAEL was 8 mg/m^3 (equivalent to an analytical concentration of 0.007 mg/L). **Portal of Entry** LOAEL was 20 mg/m^3 (equivalent to an analytical concentration of 0.017 mg/L) based on microscopic inflammatory changes in the nasal cavity Level 3, characterized by transitional respiratory epithelial hyperplasia and mixed inflammatory cell infiltration. This is a portal of entry local adverse effect. The systemic NOAEL/LOAEL was not established.
870.3465 90-Day inhalation toxicity in rats		28-day study fulfills this requirement
870.3700 Prenatal developmental in rats	46147601 (1997) Acceptable/**Guideline** w/rangefinder Primary study: 0, 50, 100, 150 mg/kg/day Rangefinder 46629401 (1996) 0, 10, 50, 100,150, 250, 500, 1000 mg/kg/day (gavage in water)	**Maternal** Systemic Toxicity NOAEL = 10 mg/kg/day (from rangefinder) Maternal Systemic Toxicity LOAEL = 50 mg/kg/day (from primary) based on clinical signs. **Developmental** Toxicity NOAEL => 150 mg/kg/day Developmental Toxicity LOAEL > 150 mg/kg/day, no treatment related effects noted in the primary study, no relevant observations in the range finding study.
870.3700 Prenatal developmental in rabbits	46207303 (2004) Acceptable/**Guideline** w/rangefinder Primary study: 0, 25, 75, 225 mg/kg/day Rangefinder: 46207302 (2003) 0, 25, 50, 100, 150, 300 mg/kg/day (gavage in water)	**Maternal** Systemic Toxicity NOAEL = 225 mg/kg/day Maternal Systemic Toxicity LOAEL = 300 mg/kg/day based on decreased bw, bwg - primary study combined with rangefinder study data **Developmental** Toxicity NOAEL = 225 mg/kg/day Developmental Toxicity LOAEL = 300 mg/kg/day based on decreased fetal bw - primary study combined with rangefinder study data
870.3800 Reproduction and fertility effects	49139201 (2013) Acceptable/Guideline 0, 20, 40 or 60 mg/kg/day	Parental and Reproductive NOAEL=60 mg/kg/day Parental and Reproductive LOAEL could not be determined Offspring NOAEL = 60 mg/kg/day Offspring LOAEL could not be determined.

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile for Furfural		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.6300 Developmental neurotoxicity		Not required
870.4100 Chronic toxicity Rats		See 870.4200
870.4100 Chronic toxicity – mice		See 870.4300
870.4200 Carcinogenicity rat. FURFURAL	46011016 (1990) Acceptable/**Non-guideline** 0, 30, 60 mg/kg/day (gavage in corn oil)	NTP 1990 Study **(publication).** Systemic Toxicity NOAEL not identified Systemic Toxicity LOAEL = 30 mg/kg/day based on liver histopathology (increased incidence of centrilobular necrosis) "Likely to be Carcinogenic to Humans" Cholangiocarcinomas of liver (male rats)
870.4200 Carcinogenicity rat. FURFURYL ALCOHOL	49161601 (1999) Acceptable/Guideline 0, 2, 8 or 32 ppm	NTP 1999 Study **(publication).** Systemic Toxicity NOAEL not identified Systemic Toxicity LOAEL = 2 ppm based nasal lesions in both sexes "Likely to be Carcinogenic to Humans" Nasal tumors (male rats)
870.4300 Carcinogenicity mouse. FURFURAL	46011016 (1990) Acceptable/**Non-guideline** 0, 50, 100, 175 mg/kg/day	NTP 1990 Study **(publication)** Systemic Toxicity NOAEL =50 mg/kg/day Systemic Toxicity LOAEL =100 mg/kg/day based on non-neoplastic liver lesions (chronic inflammation in both sexes and increased hepatic pigmentation in males) Limited parameters measured. "Likely to be Carcinogenic to Humans" Liver tumors (both sexes)
870.4300 Carcinogenicity mouse. FURFURYl ACOHOL	46011016 (1990) Acceptable/**Non-guideline** 0, 50, 100, 175 mg/kg/day	NTP 1990 Study **(publication)** Systemic Toxicity NOAEL =100 mg/kg/day Systemic Toxicity LOAEL =175 mg/kg/day based on non-neoplastic liver lesions (chronic inflammation and increased hepatic pigmentation in both sexes). Limited parameters measured. "Likely to be Carcinogenic to Humans" Kidney tumors (male mice)

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile for Furfural		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Gene Mutation 870.5100	46011017 (1999) Acceptable/**Guideline**	Negative for bacterial reverse mutation assay
Gene Mutation 870.5100	46011018 (2003) Acceptable/**Non-guideline**	Negative for *in vivo* gene mutation bacterial gene incorporation into genome of transgenic mice
CA/SCE 870.5375, 870.5385, 870.5900, 870.5915	46011019 (2003) Compilation of 7 reports	Negative and Acceptable/Guideline: Reverse Gene Mutation, In vitro mammalian gene mutation and chromosomal aberrations , In vivo Chromosomal Aberrations, SCE, Gene Mutation – Drosophilia **Unacceptable**/Guideline – Expert Panel Report, SCE in human Lymphocytes, in vitro cytogenetic assays
UDS 870.5500, 870.5560	46011020 (2003) Compilation of 9 reports	Negative for DNA damage/repair, rec-assay, UDS in rat hepatocytes – Acceptable/Guideline DNA damage, summary reports - **Unacceptable**
870.7485 Metabolism and pharmacokinetics	47750502 (1992) Acceptable/**Non-guideline** 0.127, 1.15, 12.5 mg/kg (gavage in corn oil)	Furfural was rapidly absorbed and eliminated at all dose levels (80% within 24 hours, 85% within 72 hours out of a recovery of 90%). The urine was the major route of elimination (85% within 72 hours). Minor routes were feces (<2%) and exhalation as carbon dioxide (<7%). Furfural was retained in tissues at low levels of less than 1% of the administered dose (range 0.1 ± 0.1% at 0.127 mg/kg to 0.6 ± 0.1% at 12.5 mg/kg), indicating low potential for bioaccumulation.
870.7600 Dermal penetration		None.
870.7800 28-day Immunotoxicity in rats	48999301 (2012) Acceptable/Guideline 0, 20, 40, 60, 80 mg/kg/day	NOAEL for systemic toxicity = 80 mg/kg/day LOAEL for systemic toxicity could not be determined. NOAEL for immunotoxicity = 80 mg/kg/day LOAEL for immunotoxicity could not be determined.

Non-guideline = studies either from the open literature, studies not meeting guideline requirements, but contain useful information or range-finding studies

A.3 Hazard Identification and Endpoint Selection

A.3.2 Acute Reference Dose (aRfD) - General Population

Study Selected: Acute Neurotoxicity Study

MRID No.: 48998502 (main); 48998501 (range-finding)

Executive Summary: See Appendix A. Guideline §870.6200a

Dose and Endpoint for Establishing aRfD: The NOAEL = 80 mg/kg/day based on mortality and effects on FOB parameters and motor activity in males and females seen at the LOAEL of 200 mg/kg/day.

Uncertainty Factor (UF): 100x (10X intraspecies variation, 10X interspecies extrapolation)

Comments about Study/Endpoint/Uncertainty Factor: The effects observed were the result of a single dose and are appropriate for the population of concern (general population).

$$\textbf{Acute RfD} = \frac{\textbf{80 mg/kg (NOAEL)}}{\textbf{100 (UF)}} = \textbf{0.8 mg/kg}$$

A.3.3 Chronic Reference Dose (cRfD)

Study Selected: 2-Year Rat Feeding

MRID No.: 46011016

Executive Summary: See Appendix A. OPPTS §870.4100 OPP §83-1

Dose and Endpoint for Establishing cRfD: A systemic toxicity NOAEL was not identified. Therefore, a LOAEL of 30 mg/kg/day, based on liver pathological observations (increased incidence of centrilobular necrosis), is appropriate for the chronic dietary assessment.

Uncertainty Factor(s): 300x (10X intraspecies variation, 10X interspecies extrapolation, 3X for extrapolation from a LOAEL to a NOAEL).

Comments about Study/Endpoint/Uncertainty Factor: The route and duration of exposure are appropriate for assessing chronic dietary risk.

$$\textbf{Chronic RfD} = \frac{\textbf{30 mg/kg/day (LOAEL)}}{\textbf{300(UF)}} = \textbf{0.1 mg/kg/day}$$

A.3.4 Incidental Oral Exposure (Short –Term and Intermediate-Term)

Incidental oral endpoints were selected for mouthing scenarios for children playing on treated athletic fields.

Study Selected: Prenatal Developmental Toxicity - Rat

MRID No.: 46147601 and 46629401

Executive Summary: See Appendix A. OPPTS § 870-3700; OPP §81-3

Dose and Endpoint for Establishing aRfD: Maternal NOAEL of 10 mg/kg/day, based on clinical signs of toxicity (bilateral exophthalmia, tremors, and head held low) at 50 mg/kg/day.

Level of Concern for MOE: 100
The MOE of 1000 is comprised of the 10X intraspecies variation factor, 10X interspecies extrapolation factor, and 10x database uncertainty factor.

Comments about Study/Endpoint/Uncertainty Factor: Clinical signs of toxicity were observed after repeat dosing from GD 6-15, which is appropriate for both the short- and intermediate-term durations. It is noted that this endpoint is applicable to both adults and to the young. No effects were seen in the offspring in the 2-generation reproduction toxicity study in rat up to 60 mg/kg/day.

A.3.5 Dermal Absorption

A dermal absorption study was not provided to the agency.

An estimated dermal absorption factor of 10% was derived from the ratio of the maternal LOAEL of 50 mg/kg/day from the developmental rat study to the LOAEL of 500 mg/kg/day from the 28-day dermal toxicity study.

A.3.6 Dermal Exposure (Short-, and Intermediate-Term)

The furfural use pattern currently suggests an exposure potential for the short- and intermediate-term durations. The current use profile does not support a long-term exposure assessment. Therefore, a long-term dermal endpoint has not been identified.

Study Selected: 28-Day Repeat Dermal in Rats

MRID. No.: 46917201 and 46917202

Executive Summary: See Appendix A. Guideline §870.3200

Dose and Endpoint used for risk assessment: Systemic Toxicity NOAEL is 250 mg/kg/day. Systemic LOAEL is 500 mg/kg/day based on adverse clinical signs (males), an increase in

motor activity (males) and increased mortality (males and females). There was no indication of dermal irritation in this or the other subchronic dermal toxicity study.

Occupational/Residential Level of Concern (LOC): 100
The occupational LOC for MOE is 100 due to the 10X inter-species extrapolation factor and the 10X intra-species variability factor.

Comments about Study/Endpoint and Uncertainty Factor: The endpoint selected is based on a study with the proper route and duration of exposure for both short- and intermediate-term dermal assessments.

Dermal Exposure (Long-Term)

Long-term dermal exposure is not anticipated based on the current use profile.

A.3.7 Inhalation Exposure (See Appendix B for HEC assessment array)

As stated previously, in addition to occupational handlers' exposure to furfural via the inhalation route, furfural has the potential to move off site from the area of application. Individuals near a site of furfural application (bystanders), therefore, may inadvertently become exposed to furfural through ambient air. Data for other volatile chemicals (e.g., fumigants) indicate that acute inhalation exposures to bystanders and workers typically present the greatest risk concern. This is due to the concentration of the chemical as it moves off of the field. Public health data for other volatile chemicals suggest that bystander exposure results mainly from this migration via air. Therefore, endpoints have been identified for the occupational as well as bystander assessments.

In evaluating the risks that a compound may pose to human health after exposure *via* the inhalation route, different methodologies have been historically used by the USEPA. The Agency's current approach to calculating risks due to inhalation exposure is based on the guidance methodology developed by the Office of Research and Development (ORD) for the derivation of inhalation reference concentrations (RfCs) and human equivalent concentrations (HECs) for use in margin of exposure (MOE) calculations. Under this approach, endpoint selection is based on the endpoints occurring at the lowest HECs (which may or may not be the lowest animal NOAEL). This methodology is consistent with the methodologies employed for the other soil fumigant compounds. Furthermore, the following endpoints for the inhalation scenarios reflect the conclusions of the HED ToxSAC (1-7-10).

Based on the current use pattern, acute and short-/intermediate-term inhalation exposures were calculated for both non-occupational (bystander) and occupational exposures. The acute HECs are identical for non-occupational and occupational exposure (e.g., 6.63 mg/m^3) because they are based on acute, reversible effects, with no need for adjustment in hours of exposure per day or days per week. The differences in short- and intermediate-term HECs for non-occupational versus occupational exposures arise because it is presumed, and the most conservative estimate, that non-occupational exposure (bystanders in their homes) may occur 24 hours/day, 7 days/week. In contrast, occupational exposure is presumed to occur only during the course of an

average workweek (8 hours/day and 5 days/week). The movement of furfural from the site of application is very rapid, within 6 hours. Therefore, the duration of exposure to furfural in the HEC calculations were adjusted to reflect this 6 hour exposure instead of the typical 24-hour bystander and 8-hour worker durations. A Systemic HEC is not appropriate since there are no systemic effects identified in either of the inhalation studies. Nasal irritation was more sensitive than any systemic endpoints via the inhalation route of exposure. The HEC array table reflects the time adjustment in the calculations (Appendix B)

Acute Inhalation Exposure

Study Selected: Acute Inhalation Toxicity Study with Complete Recovery – Non-guideline.

MRID. No.: 48563701

Executive Summary: See Appendix A.

Short-/Intermediate-Term Inhalation Exposure

Study Selected: Subchronic Inhalation Toxicity - Rat; OPPTS 870.3465 [§82-4]; OECD 413.

MRID. No.: 47419101

Executive Summary: See Appendix A.

Non-Occupational (Acute, Short-, and Intermediate)

Table 3.1.: Table of port-of-entry endpoints for non-occupational (bystander) exposure based on an acute inhalation rat study with NOAEL 40 mg/m^3 and a 28-day inhalation rat study with NOAEL 8 mg/m^3 and LOAEL of 20 mg/m^3	
Effect Endpoint	**HEC**
Acute Bystander	
extrathoracic (ET)	1.69 ppm (6.63 mg/m^3)
tracheobronchial (TB)	No effect identified from study
pulmonary (PU)	No effect identified from study
Systemic	No effect identified from study
The portal-of-entry LOAEL was not observed.	
Short- and Intermediate-Term Bystander	
extrathoracic (ET)	0.24 ppm (0.95 mg/m^3)
tracheobronchial (TB)	No effect identified from study
pulmonary (PU)	No effect identified from study
Systemic	No effect identified from study
The port-of-entry LOAEL 20 mg/m^3 is based on the incidence of microscopic lesions (transitional respiratory epithelial hyperplasia) and mixed inflammatory cell infiltration of the nasal cavity (Nasal Levels II-III).	

Dose and endpoint used for risk assessment:

Acute Bystander: A 6-hour HEC of 1.69 ppm (6.63 mg/m^3), based on lesions in the nose (observed only for males) at concentration levels of 20 mg/m^3 and above at one day following inhalation. A gradient was observed ranging from very slight/slight transitional epithelial hyperplasia and inflammation (Levels I-II) at the anterior levels, to slight/very slight inflammation in the more posterior levels of the nose (Levels III-VI), along with one occurrence of slight multifocal olfactory epithelial degeneration in Level VI. The nasal lesions were fully reversible within 2 weeks following a single inhalation exposure at concentrations up to 40 mg/m^3. Protection of nasal irritation likely also protects against other changes deeper in the respiratory tract. An MOE of 30 defines HEDs level of concern in accordance with the guidance provided in the RfC methodology (see RfC Uncertainty Section below and Appendix B, Table1B for HEC calculations).

Short- and Intermediate-Term Bystander: A 6-hour HEC of 0.24 ppm (0.95 mg/m^3), based on the incidence of microscopic lesions (transitional respiratory epithelial hyperplasia) and mixed inflammatory cell infiltration of the nasal cavity (Nasal Levels II-III) in the repeat inhalation study, which provides the most sensitive endpoint for the inhalation assessment, nasal irritation. Irritation of the nasal cavity did resolve by 4 weeks post-exposure. It is not known, however, whether the time required for complete recovery is significantly less than 4 weeks. Protection of nasal irritation likely also protects against other changes deeper in the respiratory tract. An MOE of 30 defines HEDs level of concern in accordance with the guidance provided in the RfC methodology (see RfC Uncertainty Section below and Appendix B, Table1B for HEC calculations).

Occupational (Acute, Short-, and Intermediate)

Table 3.2.: Table of port-of-entry endpoints for occupational exposure based on an acute inhalation rat study with NOAEL 40 mg/m^3 and a 28-day inhalation rat study with NOAEL 8 mg/m^3 and LOAEL of 20 mg/m^3	
Effect Endpoint	**HEC**
Acute Occupational	
extrathoracic (ET)	1.69 ppm (6.63 mg/m^3)
tracheobronchial (TB)	No effect identified from study
pulmonary (PU)	No effect identified from study
Systemic	No effect identified from study
The portal-of-entry LOAEL was not observed.	
Short- and Intermediate-Term Occupational	
extrathoracic (ET)	0.34 ppm (1.33 mg/m^3)
tracheobronchial (TB)	No effect identified from study
pulmonary (PU)	No effect identified from study
Systemic	No effect identified from study
The port-of-entry LOAEL 20 mg/m^3 is based on the incidence of microscopic lesions (transitional respiratory epithelial hyperplasia) and mixed inflammatory cell infiltration of the nasal cavity (Nasal Levels II-III).	

Acute Occupational: A 6-hour HEC of 1.69 ppm (6.63 mg/m^3), based on lesions in the nose (observed only for males) at concentration levels of 20 mg/m^3 and above at one day following inhalation. A gradient was observed ranging from very slight/slight transitional epithelial hyperplasia and inflammation (Levels I-II) at the anterior levels, to slight/very slight inflammation in the more posterior levels of the nose (Levels III-VI), along with one occurrence of slight multifocal olfactory epithelial degeneration in Level VI. The nasal lesions were fully reversible within 2 weeks following a single inhalation exposure at concentrations up to 40 mg/m^3. Protection of nasal irritation likely also protects against other changes deeper in the respiratory tract. An MOE of 30 defines HEDs level of concern in accordance with the guidance provided in the RfC methodology (see RfC Uncertainty Section below and Appendix B, Table1B for HEC calculations).

Short- and Intermediate-Term Occupational: A NOAEL of 8 mg/m^3, based on the incidence of microscopic lesions (transitional respiratory epithelial hyperplasia) and mixed inflammatory cell infiltration of the nasal cavity (Nasal Levels II-III) at the LOAEL of 20 mg/m^3. The duration of exposure in the 28-day inhalation toxicity study is appropriate for short- and intermediate-term risk assessments and it yields the lowest HEC (*ie*. most health-protective exposure concentration) for these exposure scenarios. It is not known, however, whether the time required for complete recovery is significantly less than 4 weeks. Protection of nasal irritation likely also protects against other changes deeper in the respiratory tract. For occupational handler exposure, the LOC is for an MOE of 100 because the RfC methodology was not employed to convert concentration of 8 mg/m^3 to a dose of 2.09 mg/kg/day. Instead the following approach was used: Dose (mg/kg/day) = (NOAEL (8 mg/m^3) * conversion factor (0.001 m^3/L) * Respiration rate of a young adult Sprague-Dawley rat (10.26 L/hr) * Study daily exposure duration (6 hr/day)) / Body weight of a young adult Sprague-Dawley rat (0.236 kg).

Long-term Inhalation Exposure

HED believes that chronic furfural exposure is unlikely based on the current proposed use pattern. Chronic inhalation studies are currently unavailable for furfural. Therefore, a long-term inhalation exposure assessment is not appropriate for furfural at this time.

Uncertainty Factors for RfC Methodology

When conducting inhalation risk assessments, the magnitude of the uncertainty factors (UFs) applied is dependent on the methodology used to calculate risk. For studies in this risk assessment with inhalation animal data, UFs are based on the RfC methodology developed by the Office of Research and Development (ORD) for the derivation of inhalation reference concentrations (RfCs) and human equivalent concentrations (HECs) for use in margin of exposure (MOE) calculations. Since the RfC methodology takes into consideration the pharmacokinetic (PK) differences, but not the pharmacodynamic (PD) differences, the UF for interspecies extrapolation may be reduced to 3X (to account for the PD differences) while the UF for intraspecies variation is retained at 10X [Note: A 3X UF for interspecies extrapolation is retained to account for the PD differences between animals and humans which are not accounted for in the RfC methodology]. Thus, the total UF when using the RfC methodology is customarily 30X.

A.4 Executive Summaries

A.4.1 Subchronic Toxicity

870.3100 90-Day Oral Toxicity – Rat and Mouse

In two independent studies (MRID 46011015) conducted under the U.S. National Toxicology Program (NTP), Furfural (99% a.i.; Lot # Q112979) was administered for up to 13 weeks in corn oil via gavage to 10 F344/N rats/sex/group at nominal dose levels of 0, 11, 22, 45, 90 or 180 mg/kg/day or 10 $B6C3F_1$ mice/sex/group at 0, 75, 150, 300, 600, or 1200 mg/kg/day. The dosages were administered daily 5 days/week at dose volumes of 5 mL/kg in the rats and 10 mL/kg in the mice. Survival, body weight, body weight gain, and organ weight data were provided. Histopathology liver findings were summarized in the text. The stated purpose of the studies was to evaluate cumulative toxic effects of furfural and to determine the doses to be used in the carcinogenicity studies.

In the rat study, 9/10 males and 10/10 females in the 180 mg/kg group, and 1/10 males and 4/10 females in the 90 mg/kg group died before the end of the study. The majority of the 90 mg/kg deaths were due to gavage injury. Mean body weights and body weight gains were similar to controls; terminal body weights were only slightly increased (p less than or equal to 0.05) in the 45 and 90 mg/kg males compared to controls. In the 90 mg/kg male rats, increases (p less than or equal to 0.05) in absolute and relative (to body) liver weights were observed. A non-dose dependent increase in the incidence of minimal to mild hepatocyte cytoplasmic vacuolization was observed in controls and all treated males (9-10/10 treated vs 4/10 controls). Based on this study, the NTP selected 60 mg/kg/day as the high dose and 30 mg/kg/day as the low dose for the subsequent two year rat study.

The Systemic Toxicity NOAEL is 45 mg/kg/day and the Systemic Toxicity LOAEL is 90 mg/kg/day based on liver weight changes and liver pathological observations. The observation data available in this study for endpoint determination was minimal, this study was used as a range-finding study for the NTP carcinogenesis study.

In the mouse study, all animals that received 1200 mg/kg and the majority of the 600 mg/kg group died within the first few weeks of the study. These deaths were considered treatment-related. At 150 and 300 mg/kg, mean body weights, body weight gains, and terminal body weights were slightly decreased in the males and were similar to controls in the females. Increased (p less than or equal to 0.05) relative (to body) liver weights were observed in the 300 mg/kg males and the 75, 150, and 300 mg/kg females. It was stated that centrilobular hepatocyte coagulative necrosis was observed in the 1200 mg/kg group (8/10 males and 2/10 females) and in males at 600 mg/kg (9/10), 300 mg/kg (1/10), and 150 mg/kg (1/10). Inflammation, characterized by a minimal to mild mononuclear inflammatory cell infiltrate, was also observed in the presence of liver necrosis. Based on this study, the NTP selected 175 mg/kg/day as the high dose and 50 mg/kg/day as the low dose for the subsequent mouse carcinogenicity study.

The Systemic Toxicity NOAEL was not observed and the Systemic Toxicity LOAEL is 75 mg/kg/day (lowest dose tested) based on liver weight changes and liver pathological observations. The observation data available in this study for endpoint determination were minimal, this study was used as a range-finding study for the NTP carcinogenesis study.

These studies do not completely satisfy the guideline recommendations for a subchronic oral toxicity study in rodents (OPPTS §870.3100; OPP §82-1); however, the data are supportable for use in the choice of regulatory endpoints with appropriate uncertainty factors. These studies were used as range-finding studies for the NTP carcinogenesis studies.

870.3150 90-Day Oral Toxicity – Dog

None.

870.3200 21/28-Day Dermal Toxicity – Rat

MRID # 46465501: 28-Day Dermal Toxicity - Rats

Bhoite, P.Y. (2004) Repeated Dose 28-Day Dermal Toxicity Study of Furfural in Rats Followed by a 4-Week Recovery Period. Jai Research Foundation, Department of Toxicology, Gurat, India. Study Number 4700, December 03, 2004.

In a 28-day dermal toxicity study (MRID 46465501), technical liquid furfural (98.48% a.i), batch labeled as Dec. 2003, was applied to the shaved skin of Wistar rats (10/sex/dose) at dose levels of 0, 25, 50 and 100 mg/kg bw/day, 6 hours/day, 5 days/week during a 28-day period. The controls animals received applications of water only. These treatment animals were designated as G1, G2, G3 and G4 respectively. Two additional groups of animals (10/sex/group designated as control (G5) and high dose (G6) were treated with water or furfural during the first 4 weeks of with the treatment groups but were also retained for a 4 week post-treatment recovery period without further treatments.

All rats were observed twice daily for toxicity and weekly for body weight and food consumption. All groups were evaluated for behavioral toxicity prior to treatment and weekly thereafter to the end of their respective treatment periods. Groups G1-4 were assessed during the 4^{th} week of treatment for clinical pathology (clinical chemistry, hematology and urinalyses), groups G5 and G6, during the 4^{th} week of the recovery period. Ophthalmological examinations were performed on all rats before commencement of treatments and prior to sacrifice. At the end of the 4 week treatment period, groups G1-G4 underwent pathological examination for organ weight changes, gross pathology and histopathological evaluation.

There were no mortalities in any of the groups, no adverse effects on body weight or food consumption; nor were there effects seen in clinical pathology or ophthalmological assessments. There were no treatment related changes in organ weights, gross pathology or histopathological changes. Skin samples apparently were not obtained for histopathology. Female rats dosed at 100 mg/kg (in both the G4 and G6 treatment groups) showed treatment related effects of drowsiness, dyspnea, clonic convulsion, hyperactivity, tremor, vocalization 3-4 hours post dosing during the first to third. These changes were not dose related or supported by weekly observations made during the four week treatment or recovery periods. The investigating laboratory carried out neurobehavioral observations without providing historical control

information to show that the laboratory had previous experience in performing neurobehavioral assessment of rats.

There were no clear cut adverse effects at the high dose level (100 mg/kg) which were supported by the results (there were no consistent clinical signs, clinical pathology and histopathological of toxicity which were seen in other studies in which furfural was administered at frankly toxic doses and which could have been seen here if the dose was high enough. The high dose levels were far below any limit dose (1000 mg/kg) which could be cited as an acceptable NOAEL if used in the study.

An LOAEL was not achieved in this study. The NOAEL was 100 mg/kg/day (highest dose tested). Aluminum foil was used to enclose the furfural liquid on the dermal application site of the rat, this is not an acceptable method.

This 28-day dermal toxicity study in the rat is unacceptable guideline study and does not satisfy the guideline requirement for a 28-day dermal toxicity study (OPPTS 870.3200 ; OECD 410) in the rat.

870.3200 21/28-Day Dermal Toxicity – Rat

In a 28-day dermal toxicity study (MRID 46917201), Furfural (99.4%, a.i., PSL No. 050401-5H) was applied to the clipped skin of 10 Crl:Wistar rats/sex/dose at dose levels of 0, 100, 250, 500, or 1000 mg/kg bw/day, 6 hours/day for 5 days/week during a 28-day period. Ten animals/sex/group were treated for the same period of time in a recovery control group and recovery high dose (1000 mg/kg) group. Due to a high incidence of mortality observed in both the high dose and high dose recovery (1000 mg/kg) groups, the dose level was lowered to 750 mg/kg on Study Day 11; however, the mortality rate remained high and cessation of treatment in this group occurred on Study Day 19. After dosing of the high dose group was terminated, surviving animals from the high dose and high dose recovery group were combined and data were collected by allowing these animals to recover until Study Day 40.

High mortality was also observed in both male and female rats dosed with 500 mg/kg/day. Before the 1000/750 mg/kg group was terminated on Study Day 19, four males and twelve females were found dead. In the 500 mg/kg group, one male and two females were found dead on Study Days 17, 19 and 23, respectively, with another male sacrificed moribund on Day 19. Clinical signs observed in males at 500 mg/kg and 1000/750 mg/kg included hypothermia, hypoactivity and hindlimb immobility. These effects were not observed in the 500 or 1000/750 mg/kg females or any of the animals in the control, 100 and 250 mg/kg group. No treatment-related effects were observed on body weight, body weight gain, food consumption, food efficiency, hematology, clinical chemistry or urinalysis parameters, and ophthalmoscopic examination. While the functional observational battery (FOB) assessments were comparable between the treated groups and controls, there was a statistically significant increase in motor activity in male rats dosed with 500 mg/kg. Those originally dosed with 1000/750 mg/kg and then allowed to recover did not exhibit increased motor activity when assessed on Study Day 39, indicating a transient effect. No dermal effects associated with treatment were observed in any of the rats.

In the animals found dead or sacrificed moribund, there were hemorrhagic lungs with corresponding lung congestion in 17/20 rats. No other treatment-related findings were identified on gross or histopathological examination.

The lowest-observed-adverse-effect level (LOAEL) for rats dosed with furfural was 500 mg/kg/day, based on adverse clinical signs (males), an increase in motor activity (males) and increased mortality (males and females). The no-observed-adverse-effect level (NOAEL) was 250 mg/kg/day.

This 28-day dermal toxicity study in the rat is **Acceptable/Guideline** and satisfies the guideline requirement for a 28-day dermal toxicity study (OPPTS 870.3200; OECD 410) in rats. Dosing was considered adequate because the high mortality precludes dosing any higher.

Non-Guideline Acute Inhalation – Rat

In an acute inhalation toxicity study (MRID 485 63701), furfural technical (99.55%, Batch No. 8902) was administered by nose-only inhalation to two groups of 5/sex/concentration Sprague Dawley rats at concentrations of 0, 10, 20, or 40 mg/m^3 for a single exposure of 6 hours in duration. The first group of animals was sacrificed the day after exposure, while the second group of animals (the recovery group) was sacrificed 14 days after exposure.

Clinical signs of toxicity, body weights, absolute and relative (to terminal body weight) lung weights, and histopathology of the respiratory tract (including six planes of section in the nose) were examined.

At one day following inhalation of furfural, lesions in the nose were observed only for males at concentration levels of 20 mg/m^3 and above. A gradient of hyperplasia and inflammation in the levels of the nose was observed. This ranged from very slight/slight transitional epithelial hyperplasia at the anterior levels that was observed in conjunction with slight/very slight inflammation (Levels I-II). In the more posterior levels of the nose (Levels III-VI) no hyperplasia was observed, however slight/very slight inflammation was observed, along with one occurrence of slight multifocal olfactory epithelial degeneration in Level VI.

This pattern is consistent with greater exposure to furfural in the anterior regions of the nose and less in the posterior regions, following the direction of inspiratory flow, and has been observed for other aldehydes (e.g. formaldehyde). Importantly, in the transitional epithelium, inflammation is a precursor to hyperplasia. This is consistent with evidence of inflammation and hyperplasia in anterior regions of the nose but inflammation only in the more posterior regions.

Two weeks after inhalation of furfural, no lesions in any of the nasal cavity regions were observed in male or female rats. This indicates that the nasal lesions observed in male rats were fully reversible within 2 weeks following a single inhalation exposure at concentrations up to 40 mg/m^3.

The LOAEL was not observed. The NOAEL is 40 mg/m^3 (0.04 mg/L).

This acute inhalation toxicity study in the rat is classified as **acceptable, non-guideline**. It does not satisfy a guideline requirement, but it is suitable for regulatory use.

870.3465 90-Day Inhalation – Rat

Muijser, J., (2001). A sub-Acute (28- Day) Inhalation Toxicity Study with Furfural in Rats.

TNO/Netherlands Organisation for Applied Scientific Reserach, Zeist, Utrechtseweg 48, The Netherlands. Laboratory Project No. 010.40657. Study No. 2874. (MRID 46426504, November 9, 2001. Unpublished. [Published report, MRID 46426505 (below)].

Arts, J.H.E, Muijser, H., Appel, M.J., et al. (2004). Subacute (28) Toxicity of furfural in Fischer 344 Rats: A Comparison of the Oral and Inhalation Route. TNO Nutrition and Food Research, Department of Toxicology and Applied Pharmacology, Zeist, The Netherlands. Study ID No. FT-12-2004-1. Food and Chemical Toxicology, vol. 42, Issue 9, September 2004, pp. 1389-1399. MRID 46426505.

In a subchronic inhalation toxicity study (MRID#'s 46426504 and 46426505), furfural (99% a.i.) commercially obtained from Sigma/Aldrich, Brussels, was administered as a vapor by the nose-only inhalation route to 5 rats/sex/group (Fischer F344 strain) initially to concentrations 0, 40, 80, 160, 320, 640, and 1280 for 6 hours per day, 5 days per week for 28 weeks. These groups were designated as Groups A to G, respectively. Additional treatment groups exposed to periods of 3 hours/day (5/sex/group) were exposed to furfural vapors at 320, 640 and 1280 mg/cu.m., 5 days per week for 28 days. These groups were designated as H, I and J, respectively. Because of excessive mortalities in groups F, G and J, this design was changed. Group F (640 mg/cu.m.) was discontinued and two new groups with fresh animals were set up: 20 mg/cu.m.for 6 hour exposures, designated herein as G2; 160 mg/cu.m.for 3 hour exposure periods, designated as J2.

Additional groups of rats (5/sex/group) were dosed by gavage with furfural dissolved in corn oil daily for 28 days to provide oral dose comparisons to the inhalation treatments over the same period of time. This DER focuses primarily on the inhalation treatments. Partial detail on the oral experiments were provided in the published report (MRID# 46426505). The oral studies are therefore only presented here in brief summary detail.

The inhalation treatment groups were evaluated daily for toxicity, weekly for body weight and food consumption, terminally for hematology changes, clinical chemistry and gross and histopathological effects.

Group F (640 mg/cu.m.) was dropped after deaths occurred during day 1 and day 8. All animals exposed to concentrations of 1280 mg/cu.m.whether for 6 hours (Group G) or for 3 hours, Group J, died in the first day of exposure. These groups were reconstituted at lower concentrations and designated G2 and J2 as noted above. There was no more mortality in the revised dosing treatments for the rest of the study.

Body weight, food consumption, and clinical pathology were not adversely affected by the inhalation treatments. Pathological changes were seen in the nasal epithelium, some seen effecting all animals at all treatment levels. Other effects were generally dose related.

Treatment related pathological effects were limited to olfactory and respiratory epithelium of the nasal cavity. There were no treatment related effects on the kidney, liver, spleen and thymus pathology. Respiratory epithelial atypical hyperplasia was seen in all treated males and females (5/5) for 6 hour exposure groups 20 mg/cu.m. to 320 mg/cu.m. (Groups G2, B, C, D, and E) and 3 hour exposure groups of 160 mg/cu.m to 640 mg/cu.m. (Groups J', H and I). Respiratory epithelial squamous metaplasia was also found in all males and female (5/5) for the same 6 hour exposure groups (G2, B, C, D and E) and all of the females (5/5) for the 3 hour exposure groups (J2, H and I) and 3-4/5 males in the same 3 hour exposure groups. Respiratory epithelial

squamous metaplasia and atypical hyperplasia were seen in males and females in a suggestive dose-response from the lowest concentration to the higher ones. Thus there were no inhalation treatments that did not result in nasal epithelium damage; however, the severity of the damage was noted to be less intense in the 3 hour exposure groups compared to the 6 hour exposure groups of animals.

The Systemic Toxicity LOAEL is 20 mg/m^3 (the lowest dose tested) based on nasal epithelial pathology seen throughout all of the treated animal groups. There was no Systemic Toxicity NOAEL established.

This subchronic inhalation toxicity study in the rat is Acceptable-Guideline and satisfies the guideline requirement for a subchronic inhalation study OPPTS 870.3465; OECD 413 in the rat.

870.3465 90-Day Inhalation – Rat

In a subchronic inhalation toxicity study (MRID 47419101), Furfural (99.68% a.i., Batch #7883) was administered as a vapor in air to 10 Sprague-Dawley rats/sex/concentration by nose-only exposure at target concentrations of 0 (air), 2, 4, 8, or 20 mg/m^3 (equivalent to analytical concentrations of 0, 0.002, 0.004, 0.007, and 0.017 mg/L, respectively) for 6 hours per day, 5 days/week for 4 weeks, for a total of 20 days of exposure. Another 5 test groups of animals (10 per sex) were exposed for the same period and kept for an observation period of 28 days, post exposure (recovery period). After 4 weeks, the main study animals (10/sex/concentration) were euthanized, and the remaining animals were sacrificed after the 4-week recovery period.

There were no reported mortalities or clinical signs of toxicity. Also there were no reported treatment related effects on body weights, food consumption, ophthalmology, hematology, clinical chemistry, organ weights, or gross pathology.

In the main study there were treatment-related microscopic findings in the nasal cavity tissues in the 20 mg/m^3 animals at sacrifice. Level 3 of the nasal cavity showed transitional respiratory epithelial hyperplasia and mixed inflammatory cell infiltration in 3 males (very slight) and 5 females (very slight to slight). In the more anterior nasal cavity (Level 2), very slight transitional respiratory epithelial hyperplasia and mixed inflammatory cell infiltration were observed in one of the aforementioned males and one of these females. Mixed inflammatory cell infiltration was observed in nasal cavity Level 2 in another of these females; however, transitional respiratory epithelial hyperplasia was not found at Level 2 in this animal. Finally, very slight mixed inflammatory cell infiltration (without transitional respiratory epithelial hyperplasia) was noted in one male (No. E176), which had no findings in nasal cavity Level 3.

In the groups with the 4-week recovery period, the only finding was at Level 3 of the nasal cavity at 20 mg/m^3, mononuclear cell infiltration in 1 male compared to 0 controls. No lesions were observed in the 20 mg/m^3 females.

The Portal of Entry LOAEL was 20 mg/m^3 (equivalent to an analytical concentration of 0.017 mg/L) based on microscopic inflammatory changes in the nasal cavity Level 3, characterized by transitional respiratory epithelial hyperplasia and mixed inflammatory cell infiltration. This is a portal of entry local adverse effect; however it is considered as potential systemic toxicity. The Portal of Entry NOAEL was 8 mg/m^3 (equivalent to an analytical concentration of 0.007 mg/L). The Systemic Toxicity NOAEL/LOAEL was not established in this study.

At the request of the Agency, this study was conducted for 28 days, instead of the 90 days recommended by Guideline OPPTS 870.3465. Aside from the different study duration, this study was conducted in accordance with Guideline OPPTS 870.3465.
This 28-day study is classified as **acceptable/guideline** and as such satisfies the guideline requirement (OPPTS 870.3465; OECD 413) for a subchronic inhalation study in the rat.

A.4.2 Prenatal Developmental Toxicity

870.3700a Prenatal Developmental Toxicity Study - Rat

In a developmental toxicity study (MRID 46147601), Furfural technical (99.4-100% a.i., Lot # 1218) was administered daily via oral gavage to 25 presumed pregnant Sprague-Dawley (Crl:CD®(SD)BR) rats/group at a dose volume of 5 mL/kg (in water) at dose levels of 0, 50, 100, or 150 mg/kg/day from gestation day (GD) 6 through 15. In the 150 mg/kg/day group, dosing was terminated on April 15, corresponding to GD 10-14, due to substantial maternal toxicity. However, the rats in this group remained on study to assess reversibility. All surviving dams were killed on GD 20; their fetuses were removed by cesarean section and examined.

Between GD 6 and 15, 3/25 dams in the 100 mg/kg/day group died, and 16/25 dams in the 150 mg/kg/day group died. Among the decedents, foamy contents in the trachea and firm lungs were noted in 1/3 dams at 100 mg/kg/day, and the following findings were noted at 150 mg/kg/day: (i) foamy contents in the trachea and firm lungs in 2/16 dams; (ii) mottled or dark red lungs in 3/16 dams; (iii) dilated renal pelvis in 2/16 dams; (iv) dark red contents in the jejunum in 1/16 dams; and (v) autolyzed intestine and complete litter resorption in 1/16 dams.

At one hour post-dosing, the following clinical signs of toxicity were observed: (i) bilateral exophthalmia, tremors, and head held low at 50 mg/kg/day and above; (ii) hypoactive, vocalization, labored respiration, rales, gasping, and rapid respiration at 100 mg/kg/day and above; and (iii) prostrate, lethargic, limited use of hindlimbs, and dried red material around mouth and right eye at 150 mg/kg/day.

During the daily clinical examinations, bilateral exophthalmia was observed at 50 mg/kg/day and above. Additionally at 150 mg/kg/day, the following clinical signs of toxicity were noted: (i) hypoactive; (ii) prostrate; (iii) tremors; (iv) head held low; (v) labored/rapid respiration; (vi) rales; (vii) decreased defecation; (viii) unkempt appearance; and (ix) numerous findings on the coat and around the eyes, nose, and mouth, including matting (clear, yellow, brown, red, wet, or dry) on the forelimbs and ventral thoracic, abdominal, and/or urogenital areas.

At 150 mg/kg/day, body weight gains and absolute and relative (to body weight) food consumption were decreased during GD 6-12, resulting in decreased body weight gains for the overall (GD 6-16) treatment interval. Body weight gains and food consumption in this group were comparable to controls during GD 12-16, corresponding to when the surviving animals in this group were taken off dose (GD 10-14).

The Maternal Toxicity NOAEL is less than 50 mg/kg/day and the Maternal Toxicity LOAEL is equal to or less than 50 mg/kg/day based on clinical signs of toxicity (bilateral exophthalmia, tremors, and head held low).

There were no effects of treatment on the mean numbers of corpora lutea, implantations, or live fetuses per dam. Similarly, in animals surviving to scheduled sacrifice, there were no abortions, premature deliveries, dead fetuses, or complete litter resorptions, and there were no effects of treatment on the number of resorptions (early or late) or on fetal weights, sex ratio, or post-implantation loss. There were no treatment-related external, visceral, or skeletal malformations or variations.

The Developmental Toxicity NOAEL is equal to or greater than 150 mg/kg/day and the Developmental Toxicity LOAEL is greater than 150 mg/kg/day.

A Maternal Toxicity NOAEL in the primary study was not established; therefore, the doses selected for this primary study were apparently too high. It was stated that the dose levels were selected based upon the results of a preliminary range-finding study (Study # WIL-12377), this study used dose levels ranging from 10 to 1000 mg/kg/day. The comparable doses between the 2 studies were the 50, 100 and 150 mg/kg/day, based on the effects noted in the range-finding study at 150 mg/kg/day which included clinical signs and transient body weight decrease, a supportable Maternal Toxicity NOAEL of 10 mg/kg/day can be established.

This study is classified **Acceptable-Guideline** and satisfies the guideline requirements for a developmental study in the rat **(OPPTS 870.3700a/OPP 83-3a)** when used with the range-finding study (Study # WIL-12377).

870.3700b Prenatal Developmental Toxicity Study - Rabbit

In a developmental toxicity study (MRID 46207303), Furfural technical (99.67% a.i., Lot # 0305-1373A) was administered daily via oral gavage to 25 artificially inseminated New Zealand White rabbits/group at dose levels of 0, 25, 75, or 225 mg/kg/day at a dose volume of 5 mL/kg from gestation day (GD) 0 through 28. All surviving does were killed on GD 29; their fetuses were removed by cesarean section and examined.

There were no effects of treatment on survival, body weights, body weight gains, net body weight gain (adjusted for gravid uterine weight), gravid uterine weight, absolute or relative (to body weight) food consumption, or gross pathology.

The only apparent effect of treatment was the observation of unkempt appearance in 1/24 rabbits at 75 mg/kg/day for 8 days and in 6/25 rabbits at 225 mg/kg/day for an average of 4.3 days per rabbit. Since this clinical sign was not corroborated by any other findings, it is not considered toxicologically significant.

The Maternal Toxicity NOAEL is equal to or greater than 225 mg/kg/day and the Maternal Toxicity LOAEL was not established.

A Maternal Toxicity LOAEL in the primary study was not established; therefore, the doses selected for this primary study were apparently too low. It was stated that the dose levels were selected based upon the results of a preliminary range-finding study (MRID 46209401) with dose levels of 0, 25, 50, 100, 150, and 300 mg/kg/day (See Executive Summary below). The comparable dose between the 2 studies was 25 mg/kg/day. Based on the effects noted in the range-finding study at 300 mg/kg/day which included decreased body weight/body weight gain a supportable Maternal Toxicity LOAEL of 300 mg/kg/day

can be established combining the range-finding study and the main study.

There were no dead fetuses or premature deliveries. Similarly, there were no effects of treatment on the pregnancy rate, sex ratio, pre-implantation loss, post-implantation loss, or on the numbers of abortions, corpora lutea, implantations, litters, live fetuses, or resorptions (early, late, or complete litter). There were no effects of treatment on fetal body weights or on ossification of the skeleton, indicating that fetal growth and development were unaffected by treatment. There were no treatment-related external, visceral, or skeletal malformations or variations.

The Developmental Toxicity NOAEL is 225 mg/kg/day and the Developmental Toxicity LOAEL was not established.

A developmental toxicity LOAEL in the primary study was not established; therefore, the doses selected for this primary study were apparently too low. It was stated that the dose levels were selected based upon the results of a preliminary range-finding study (MRID 46209401) with dose levels of 0, 25, 50, 100, 150, and 300 mg/kg/day (See Executive Summary below). The comparable dose between the 2 studies was 25 mg/kg/day. Based on the developmental effects noted in the range-finding study at 300 mg/kg/day which included decreased fetal body weight, a supportable developmental toxicity LOAEL of 300 mg/kg/day can be established combining the range finding study and the main study.

NOTE: Although neither a Maternal nor a Developmental Toxicity LOAEL was observed in the primary study, Maternal Toxicity was observed at 300 mg/kg/day in the range-finding study. Thus, the dose selection rationale for the definitive study was appropriate.

This study is classified **Acceptable/Guideline** and, in conjunction with the range-finding study (MRID 46207302) (see below), satisfies the guideline requirements for a developmental study in the rabbit **(OPPTS 870.3700b; OPP 83-3b)**.

Range-Finding Study: In a developmental toxicity study (MRID 46207302), Furfural technical (99.8% a.i., Lot # 5215) was administered daily in deionized water via oral gavage to 6 artificially inseminated New Zealand White rabbits/group at dose levels of 0, 25, 50, 100, 150, or 300 mg/kg/day at a dose level of 5 mL/kg from gestation day (GD) 0 through 28. All surviving does were killed on GD 29. Their fetuses were removed by cesarean section and examined for external abnormalities and discarded; visceral and skeletal examinations were not performed.

At 300 mg/kg/day, one female (#37615) was euthanized in extremis on GD 15. This doe had decreased food consumption (≤5 g/day) on GD 5-15, resulting in emaciation by GD 15. Decreased defecation and small feces was noted in this animal from GD 1-15. All other does survived to scheduled termination.

Decreased defecation and small feces was also noted in all treatment groups, but occurred at a low frequency and in a manner unrelated to dose at 25, 50, 100, and 150 mg/kg/day. At 300 mg/kg/day, decreased feces was observed in 5 does for an average of 8.4 days/rabbit; and small feces was noted in 5 does for an average of 5.6 days/rabbit. There were no other treatment-related clinical signs in the daily observations, and no clinical signs of toxicity were noted at 1-hour post-dosing.

At 300 mg/kg/day, body weights were decreased (↓4-11%; not significant [NS]) during GD 1-15. Body weight gains were decreased during GD 0-7 (↓90%; $p \leq 0.05$), GD 7-14 (↓122%; NS), and

for the overall (GD 0-29) study (↓28%; NS). Gravid uterine weights were decreased by 21% (NS) compared to controls. Absolute and relative (to body weight) daily food consumption were decreased (↓33-51%; $p \leq 0.05$) generally between GD 0-18. Absolute food consumption was decreased (↓41-45%; $p \leq 0.05$) for GD 0-7 and 7-14, and relative (to body weight) food consumption was decreased (↓28-44%; $p \leq 0.05$) for GD 0-7, 7-14, and 14-21.
At 300 mg/kg/day, the cesarean section examinations revealed decreases in the mean numbers of gravid females (3/6 treated vs 6/6 controls), corpora lutea (7.0 treated vs 10.8 controls), and viable fetuses (3.3 treated vs 4.5 controls) and increases in the mean numbers of early resorptions (1.3 treated vs 0.2 controls) and late resorptions (1.0 treated vs 0 controls), resulting in increased post-implantation loss (2.3% in treated vs 0.2% in controls). There were no treatment-related external findings in the fetuses.

The dose selection for the primary study were 0, 25, 75, and 225 mg/kg/day since there were reduced fetal body weights at 150 mg/kg/day and more severe toxicity at 300 mg/kg/day.

A.4.3 Reproductive Toxicity

870.3800 Reproduction and Fertility Effects - Rat

In a two-generation reproduction study (MRID 49139201), Furfural (100% a.i., lot # 20111216) in a deionized water vehicle was administered by gavage to groups of 30 sexually mature male and 30 virgin female F_0 and F_1 Crl:CD(SD) rats at dose levels of 0, 20, 40, or 60 mg/kg bw/day. F_0 and F_1 males were dosed daily for 70 days premating and during and after mating until sacrificed after weaning the F_1 and F_2 litters, respectively. F_0 and F_1 females were dosed daily for 70 days premating and during mating, gestation, and lactation until sacrificed after weaning their litters. Each parental generation produced only one litter. Parental systemic toxicity, reproductive function and performance, and offspring viability, growth, and sexual maturation were evaluated in this study.

No test substance-related effects were observed on the systemic parental parameters evaluated in F_0 or F_1 rats in this study (mortality, clinical signs, body weight, body weight gain, food consumption, food efficiency, macroscopic and microscopic findings, and organ weights). No test substance-related effects were observed on parameters of reproductive function and performance in F_0 or F_1 rats in this study (estrous cycle periodicity and length, pre-coital and gestation intervals, sperm motility and progressive motility, concentration of sperm in the epididymis, sperm production rate, spermatid morphology, male and female mating and fertility indices, copulation index in males, conception index in females, total litter loss, number of live born litters, macroscopic and microscopic findings in reproductive organs).

The lowest-observed-adverse-effect level (LOAEL) for parental and reproductive toxicity for furfural in rats could not be determined from this study. The NOAEL is 60 mg/kg/day for this study.

No test substance-related effects were observed on offspring parameters evaluated F_1 or F_2 pups during lactation (number of pups born alive, number of dead pups, sex ratio at birth, live birth and viability indices, macroscopic findings, and age and weight at sexual maturation).

The lowest-observed-adverse-effect level (LOAEL) for offspring toxicity for furfural in rats could not be determined from this study. The NOAEL is 60 mg/kg/day for this study.

This study is A**cceptable/Guideline** and it does satisfy the guideline requirements for a two-generation reproduction and fertility study (OCSPP 870.3800; OECD 416) in rats.

A.4.4 Chronic Toxicity

870.4100a (870.4300) Chronic Toxicity – Rat

See 870.4200a

870.4100b Chronic Toxicity - Dog

None.

A.4.5 Carcinogenicity

a. Furfural

870.4200a Carcinogenicity Study – rat

In a carcinogenicity study (MRID 46011016) conducted by the U.S. National Toxicology Program (NTP), furfural (99% a.i.; Lot No.: Q112979) was administered for up to 103 weeks in corn oil by **gavage** to 50 F344/N rats/sex/dose at nominal dosages of 0, 30, or 60 mg/kg/day in 5 mL/kg. Doses were administered daily (5 days/week). Survival, body weights, non-neoplastic and neoplastic histology data were reported. It was stated that these studies were conducted due to a lack of reliable data concerning the effects of long-term exposure to furfural.
In rats, no treatment-related clinical signs were observed and body weights were comparable to controls. Results of the necropsy were not presented.

A dose-dependent increase in male mortality (natural deaths and moribund kills) was observed in the rats at 30 (30%) and 60 (36%) mg/kg vs 26% in controls; however, a statistical difference was not found. Furthermore, the Kaplan-Meier survival curves showed a similar probability of survival until the final 7 weeks of the study. An increased incidence of centrilobular necrosis was observed in each treated male group (16-24% treated vs 4% controls). Additionally, focal cystic degeneration was observed in the 60 mg/kg/day males (12% treated vs 2% controls).

The Systemic Toxicity NOAEL was not established and the Systemic Toxicity LOAEL is 30 mg/kg/day based on liver pathological observations (increased incidence of centrilobular necrosis). The observational data available in this study for endpoint determination was minimal as NTP studies focus on carcinogenesis.

This study is classified as Acceptable/Nonguideline and as such does not completely satisfy the guideline recommendations for a carcinogenicity study in rats (OPPTS §870.4200; OPP §83-2); however, the data are supportable for use in the evaluation of the carcinogenetic potential of furfural.

B. Furfuryl Alcohol

870.4200a Carcinogenicity Study – rat

In a carcinogenicity study (MRID 49161601), furfuryl alcohol [>98% a.i. (lot # 7B19M-2)] was administered as a vapor in whole-body inhalation chambers to groups of 50 male and 50 female F344/N rats at concentrations of 0, 2, 8, or 32 ppm for 105 weeks. The respective mean analytical concentrations were 0, 2.01, 8.02, and 32.3 ppm based on daily measurements using an on-line gas chromatography system. The exposure concentrations were selected based on the results from a 14-week inhalation exposure study in F344/N rats. The vapor was generated in a manner that prevented particle formation using heated nitrogen, heated delivery lines, and mixing with HEPA and charcoal- filtered air. Urine was collected from five surviving rats (if available)/sex/exposure group and analyzed for the furfuryl alcohol metabolites, furoylglycine and furanacrylolglycine (volume and creatinine were also measured). Food consumption, feed efficiency, hematology, clinical chemistry, ophthalmic examination, and gross findings were not evaluated in this study.

There were no test-substance-related clinical findings during the study. Less than 25% of male rats in any exposure group, including controls, survived to the end of the study. No male rat in the high exposure group survived beyond 99 weeks which is reflected in the mean survival time of 85 weeks, and statistically lower ($p<0.001$) than the control value of 88 weeks. The cause of the low survival in males at the high dose was not addressed. The test substance did not significantly alter survival in males in the low- and mid-exposure groups or in any of the groups of exposed females. Males in the high exposure group had a 6% lower mean body weight relative to controls at week 19 and the difference progressed to -24% in week 91. Weight gain in the male high exposure group was 31% lower than controls for weeks 1-91. No significant exposure-related effect was observed on body weight or weight gain in males in the low- and mid-exposure groups or in any of the groups of exposed females. Furoylglycine and furanacrylolglycine, the two major metabolites of furfuryl alcohol, were present in the urine at concentrations approximately proportional to the exposure concentrations, indicating no concentration-related effect on the primary metabolism pathway in male rats up to 8 ppm and in female rats up to 32 ppm. Furfuryl alcohol was an obvious irritant to the nose as evidenced by increased incidences of non-neoplastic lesions relative to controls for the low- mid- and high exposure groups. The incidences of hyperplasia of the lateral wall, atrophy and metaplasia of the olfactory epithelium, and hyperplasia of the respiratory epithelium were statistically elevated at all three exposure concentrations in both sexes (typically $p\leq0.01$). The severity increased with increasing concentration to a similar extent in both males and females. However, a somewhat greater toxicity was evident in males in higher incidence rates. For example, fibrosis of the olfactory epithelium in males occurred in 1/50, 26/50, and 40/50 at 2, 8, and 32 ppm, respectively, whereas the incidences in females were 0/50, 16/50, and 31/50. The other primary target organ for non-neoplastic effects was the kidney. Statistically significant increases occurred in either the incidences or severity of nephropathy and renal tubule hyperplasia in both males and females at 32 ppm (typically $p\leq0.01$). Males in the 32 ppm group, but not females, showed a significantly increased incidence of mineralization ($p\leq0.01$). The nephropathy was more severe in males in the high exposure group (mean severity of 3.7 in males, 2.4 in females) and included parathyroid hyperplasia and osteodystrophy.

Under the conditions of this study, the systemic toxicity lowest-observed-adverse-effect-level (LOAEL) for furfuryl alcohol inhalation exposure in F344/N rats was 2 ppm based on nasal lesions in both sexes. A NOAEL was not identified.

At the concentrations tested, there was an exposure-related increase in incidence of neoplasms in the nose of exposed male rats that was statistically significant, and an increase in incidence of kidney neoplasms of exposed female rats that was not statistically significant. The nose of male rats had one (1/50) lateral wall adenoma in the 2 ppm group, one (1/50) respiratory epithelium adenoma in the 8 ppm group, and one (1/50) respiratory epithelium carcinoma, as well as three (3/50) squamous cell carcinomas in the respiratory epithelium in the 32 ppm group (squamous cell carcinoma not observed in controls or in historical controls). When the incidences of each tumor type were combined within each exposure group, the results showed the 32 ppm group of males had a statistically greater incidence relative to controls. No statistically significant findings on nasal neoplasms were observed in female rats. The microscopic examination of kidneys showed that renal tubule neoplasms were observed during the standard evaluation in both sexes of exposed rats (not statistically significant), but the incidences exceeded the historical control range of 0-2% in females. Male rat incidences using combined standard evaluation and step section data were 2/50, 2/50, 3/50, and 4/50 for renal tubule adenomas in the 0, 2, 8, and 32 ppm exposure groups, respectively. Female rat incidences were 2/49 for renal tubule adenomas at 8 ppm and 2/50 at 32 ppm, 1/49 for carcinoma at 2 ppm, and no incidence of either tumor type in the control group. The inhalation exposure concentrations were considered adequate based on the body weight effects and decreased survival observed in males in the high dose group.

This carcinogenicity study is **Acceptable/Guideline** and satisfies the Guideline requirement for a carcinogenicity study [(OCSPP 870.4200); OECD 451] in the rat. The study was a well-conducted NTP study that assessed the carcinogenic potential of inhaled furfuryl alcohol vapor in rats. It fulfilled the intent of the above Guideline but did not include all the recommended parameters. One notable deficiency was male rat survival. Survival to study termination was less than 25% for all groups of male rats, which included significantly shortened survival of males at the high concentration relative to controls. However, this deficiency appeared to be offset by use of the Poly-3 statistical test, which takes survival differences into account and does not require lethality assumptions. Several minor deficiencies are listed at the end of this document.

870.4200b Carcinogenicity (feeding) – Mouse

A. Furfural

In a carcinogenicity study (MRID 46011016) conducted by the U.S. National Toxicology Program (NTP), furfural (99% a.i.; Lot No.: Q112979), furfural was administered in corn oil vehicle to B6C3F1 mice (50/sex/dose) at dose levels of 0, 50, 100, or 175 mg/kg bw/day, 5 days/week via oral gavage for 2 years (104 weeks). Survival, body weights, non-neoplastic and neoplastic histology data were reported. In mice, no treatment-related effects were observed on body weights. It was stated that no treatment-related clinical signs were observed. Results of the necropsy were not presented.

There were no statistically significant trends for survival for male or female, but there was a survival disparity with a statistically significant pair-wise comparison of the 100 mg/kg/day mid-dose group with the controls for male mice. However, no statistically significant pair-wise comparison for survival for male mice was seen at the high dose (175 mg/kg/day). Liver toxicity in the form of chronic inflammation of the subserosa of the liver at ≥100 mg/kg/day and increased hepatic pigmentation in males (≥100 mg/kg/day) and females (175 mg/kg/day) was observed.

The Systemic Toxicity NOAEL is 50 mg/kg/day. The Systemic Toxicity LOAEL is 100 mg/kg/day based on liver toxicity (chronic inflammation of the subserosa of the liver in both sexes and increased hepatic pigmentation in males). The observational data available in this study for endpoint determination was minimal as NTP studies focus on carcinogenesis.

This study is classified as Acceptable/Nonguideline and as such does not completely satisfy the guideline recommendations for a carcinogenicity study in mice (OPPTS §870.4200; OPP §83-2); however, the data are supportable for use in the evaluation of the carcinogenetic potential of furfural.

B. Furfuryl Alcohol

In an inhalation carcinogenicity study (MRID 49161601), groups of 50 male and 50 female $B6C3F_1$ mice were exposed to furfuryl alcohol (98% a.i.; Lot # 7B19M-2) vapor by inhalation 6 hours + 12 minutes (T_{90})/day, 5 days/week for 105 weeks. The exposure concentrations were 0, 2, 8, and 32 ppm (analytical concentrations were 0, 1.99 ± 0.12, 8.01 ± 0.45, and 31.9 ± 2.07 ppm, respectively). Furfuryl alcohol was vaporized using heated nitrogen and diluted with HEPA- and charcoal-filtered air in the exposure chambers to achieve the target concentrations. The following parameters were not evaluated or reported in this study: food consumption, feed efficiency, hematology, clinical chemistry, urinalysis, and gross findings.

No exposure-related effects on survival were observed in either sex. Body weight and weight gain were not affected in male mice exposed to the test substance. Female mice in the 2-ppm group weighed 5% to 9% less than controls beginning at 59 weeks and females in the 8-ppm group weighed 7% to 9% less than controls (11% less at week 91) also beginning at week 59. Female mice in the 2- and 8-ppm groups gained 15% and 12% less weight, respectively, than controls over the entire study. Females in the 32-ppm group weighed 7% to 17% less than controls starting at week 39 and gained 21% less weight than control over the entire study.

The only exposure-related clinical sign was focal corneal degeneration in females at 32 ppm; this clinical finding corresponded with the increased incidence of corneal degeneration (26/50 vs 3/49 in controls) observed microscopically in females at 32 ppm. Female mice exposed to the test substance at 32 ppm also had increased incidences of corneal hyperplasia and chronic active inflammation that did not reach statistical significance. No effects were observed on the eyes of male mice exposed to the test substance; the effect on the eyes of female mice show that furfuryl alcohol vapor is irritating to the eyes.

Exposure-related non-neoplastic lesions were observed in the kidneys of male mice but not female mice. The severity, but not the incidence of nephropathy was slightly increased (1.8 vs 1.2 for controls) and the incidence of renal tubule degeneration was greatly increased (48/50 vs 0/50 for controls) in male mice at 32 ppm compared with that of controls. Male and female mice had increased incidences of non-neoplastic lesions in the nose including inflammation of the nasal epithelium, inflammation and hyperplasia of Bowman's gland, squamous metaplasia of the lateral wall, atrophy and metaplasia of the olfactory epithelium, hyaline degeneration and squamous metaplasia of the respiratory epithelium at 2 ppm and above. The results of this study show that furfuryl alcohol vapor is irritating and toxic to the nose of male and female mice.

The lowest-observed-adverse-effect level (LOAEL) of inhalation exposure to furfuryl alcohol vapor in mice is 2 ppm based on nasal irritation and toxicity in both sexes and decreased body weight gain in females. The no-observed-adverse-effect level (NOAEL) cannot be established from this study.

At the concentrations tested, there was an exposure-related increase in incidence of neoplasms in the kidneys of 32-ppm group male mice when compared to controls. After examination of the standard single section and step section of the kidneys, the incidence of renal tubule adenomas was 0/50, 0/49, 0/49, and 3/50, and the incidence of renal tubule carcinomas was 0/50, 0/49, 0/49, and 2/50 in male mice at 0, 2, 8, and 32 ppm, respectively. One adenoma was found during examination of the step sections bringing the total incidence of kidney tubule adenoma to 3/50. The incidence of renal tubule adenoma/carcinoma combined was 0/50, 0/49, 0/49, and 5/50 ($p \leq 0.05$). At the concentrations tested, no exposure-related neoplasms were observed in female mice. Dosing was considered adequate based on a decrease in body weight and weight gain in female mice.

This carcinogenicity study in mice is **Acceptable/Guideline** and satisfies the guideline requirements fo**r** a carcinogenicity study [OCSPP 870.4200; OECD 451] in mice. This is a well-conducted NTP study that assessed the carcinogenic potential of inhaled furfuryl alcohol vapor in mice. Although this study did not include all the recommended parameters of a guideline study, it can be used to satisfy the above guideline requirements.

A.4.6 Mutagenicity

A. Furfural

Furfural has been studied in a comprehensive battery of well-done genetic toxicology assays, many of which were sponsored by the National Toxicology Program (NTP) and are summarized below:

In Vitro Studies

Gene Mutation

As part of the NTP genetic toxicology screening of 270 chemical, furfural and furfuryl alcohol were tested by independent laboratories in the *Salmonella typhimurium* mammalian microsome mutagenicity assay using the standard plate incorporation and preincubation assays (Mortelmans *et al*., 1986). Both test material were negative in *S. typhimurium* TA100, TA1535, TA1537 or TA98 up to cytotoxic concentrations (furfural: ≥ 3333 µg/plate-S9 or + 10% rat or hamster S9) or the highest dose tested (furfuryl alcohol: 10,000 µg/plate-S9 or + 10% rat or hamster S9).

Furfural was also tested in *S. typhimurium* TA100, TA1535, TA1537, TA98 or TA102 for reverse gene mutations (MRID 46011017) at concentrations up to the limit dose for this test system (5000 µg/plate). Results were negative with or without S9 activation.

In another *Salmonella* mutagenicity assay, Marnett *et al*. (1985) found that furfural was not mutagenic in a preincubation assay with *S. typhimurium* strains TA102 or TA104 up to the maximum noncytotoxic concentration (1 µmole). These strains were used because they are more sensitive indicators of aldehyde and ketone mutagenicity than the standard Ames tester strain battery.

In contrast to the uniformly negative bacterial gene mutation assays, McGregor *et al.* (1988) demonstrated that furfural in the absence of S9 activation (an S9-activated assay was not performed), induced increases in the mutation frequency (MF) of L5178Y tk^+/tk^- mouse lymphoma cells. The response was dose-related (ranging from 1.6-fold increase at 100 µg/mL to 11.3-fold at 400 µg/mL), occurred at moderately cytotoxic concentrations (65- 11% relative total growth, RTG, respectively) and was confirmed in a repeat assay (2.3-fold increase in the MF with 27% RTG at 200 µg/mL). It is of note that when the global evaluation factor (GEF), which is a more recently accepted approach to evaluate mouse lymphoma data and is recommended by the international workshop on genotoxicity (Moore *et al*., 2002), was applied to these data, the conclusion remained positive.

Chromosome Aberrations

NTP also sponsored an *in vitro* mammalian cell chromosome aberration assay with furfural. In this study, Stich *et al.* (1981), exposed Chinese hamster ovary (CHO) cells to 0, 200, 300, 400 or 500 µg/mL -S9 for 8-10 hours or 0, 500, 760, 1000, or 1230 µg/mL +S9 for 2 hours. Due to marked cell cycle delay, cultures were harvested at 22- 23.5 hours after treatment. Metaphase analysis revealed that in the absence, but not presence, of S9-activation, the percentage of cells with chromosome aberrations was pair-wise significantly ($p<0.05$) increased at 400 and 500 µg/mL-S9 with a significant ($p<0.001$) trend.

Other Mutagenic Mechanisms

As part of the comprehensive investigation of the toxicology of furfural, NTP sponsored an *in vitro* investigation of sister chromatid exchanges (SCEs) in CHO cells. Accordingly, Stich *et al*. (1981), exposed CHO cells to 0, 11.7, 38.9 or 117 µg/mL -S9 for 8-10 hours or 0, 117, 389, or 1170 µg/mL +S9 for 2 hours. Cells were processed and second division metaphases were analyzed. All non-activated or S9-activated concentrations induced significant pairwise ($p<0.01$) and dose-related increases (trend: $p<0.001$) in the percentage SCEs/chromosomes. The response was appreciably stronger in the absence of metabolic activation.

The ability of furfural and furfuryl alcohol to induce SCEs in mammalian cells was also assayed by Gomez-Arroyo and Souza (1985). In this study, human lymphocytes, collected from healthy donors, were dosed with 3.5-14.0 x 10^{-5} M furfural or 3.3-9.9 x 10^{-3} M furfuryl alcohol for 70 hours; 50 metaphases per duplicate culture were examined and SCE frequencies were determined. Results indicated that furfural at 7.0 and 14.0 x 10^{-5} M induced significant ($p<0.001$) and dose-related increases in SCEs. By contrast, furfuryl alcohol was negative. The effect of comparable concentrations of furfural on the mitotic spindle in the human lymphocytes from healthy donors was further evaluated. Data for the 24- and 48-hour harvest intervals show significant ($p<0.001$) and dose-related increases in c-mitosis, indicative of a mitotic poison along with significant ($p<0.05$-0.001) and dose-related increased mitotic indices, indicative of stimulated cell division. The percentage of tetraploid cells was also increased significantly ($p<0.05$) at 14 x 10^{-5} M furfural but only at the 48-hour cell harvest.

Additional blood samples were collected from 6 workers occupationally exposed to furfural or furfuryl alcohol. The analysis of SCE in these workers showed no significant differences compared to the control group of 6 workers without exposure.

In Vivo Studies

In a *Drosophila melangaster* sex -linked recessive lethal mutation assay, Woodruff *et a*l. (1985) exposed 24-hour old Canton-S males to furfural either by abdominal injection (100 ppm, 24-hour recovery) or feeding (1000 ppm, 3 days). Treated males were mated with three *Basc* females for 3 days and remated with fresh females to produce three broods which sampled sperm over the entire period of spermatogenesis. A significant ($p<0.05$) increase in sex-linked recessive lethal mutations was observed in the male germ cells after injection of 100 ppm furfural. No increases were seen in the feeding phase of study. In a follow-up experiment, the same investigators found that the administration of 100 ppm via injection did not induce reciprocal translocations in *D. melanogaster* males.

In the NTP *in vivo* mouse bone marrow cytogenetic assays, furfural was neither clastogenic nor induced SCEs in the bone marrow cells of male B6C3F1 mice administered doses of 0, 50, 100 or 200 mg/kg by intrapertoneal injection.

From these data it can be concluded that there is evidence of gene mutations *in vitro* in mammalian cells (mouse lymphoma L518Y) but not in bacteria. Similarly, there is convincing evidence of chromosome aberrations (CHO cells) and SCE induction (human lymphocytes and CHO cells) *in vitro* but this genotoxic activity is not expressed *in vivo* in mouse bone marrow cells. Sex-linked recessive lethal mutations in *D. melangaster* male germinal cells were also seen following abdominal injection but not when furfural was administered via feeding for 3 days. Based on the few studies reporting evidence of gene mutations, the European Union rapporteur of the risk assessment for furfural recommended that an *in vivo* gene mutation assay should be performed to elucidate the biological relevance of the genetic toxicology results.

Accordingly, an *in vivo* gene mutation assay with λlacZ-transgenic male mice (MRID 46011018) was submitted to the Agency. In this study, five groups of 15 male transgenic mice with *lac*Z genes as the mutational target received furfural prepared in corn oil at 0, 37.5, 75, 150 or 300 mg/kg/day by oral gavage for 28 days. On Day 28, 3 mice/group were sacrificed and selected tissues (*i.e.,* liver) were collected and examined histologically. On Days 62 and 63, the remaining animals were sacrificed and genomic DNA was harvested from the liver. The *lac*Z genes were packaged in lambda phages, mixed with *Escherichia coli* C *lac*Z*rec*A*gal*E, plated and the mutation frequencies (MFs) were determined.

Dose selection was based on the findings of a 13-week subchronic toxicity study with a NOAEL of 75 mg/kg/day; 300 mg/kg/day was selected as the high dose which was expected to induce hepatotoxicity (Irwin, 1990). In the mutational assay, furfural was tested up to a toxic dose (300 mg/kg/day) based on three unscheduled deaths (3 of 10 animals), significant increases in both the absolute and relative liver weights accompanied by findings of slight centrilobular hypertrophy (3 of 3 mice), focal hemorrhage and inflammatory response (1of 3), and focal aggregates of mononuclear cells (1of 3) after 28 days of treatment. Despite the evidence of hepatotoxicity, there was no indication of a mutagenic response in the livers harvested from mice exposed for 28 days and allowed a 34 or 35 day treatment-free expression time. Based on these considerations, furfural did not induce an *in vivo* mutagenic response in this transgenic mouse test system.

Overall Conclusions for Furfural

Furfural has been studied in a comprehensive battery of acceptable genetic toxicology assays,

many of which were sponsored by the NTP, provided valuable information, and are acceptable for regulatory purposes. Furfural is uniformly negative in bacterial assays for gene mutations but is mutagenic in cultured mammalian cells (mouse lymphoma). It is also clastogenic and induces SCEs in cultured CHO cells as well human lymphocytes. It is of note that the genotoxic response is more apparent in the absence rather than the presence of exogenous rodent metabolic activation. This observation is consistent with the negative findings from assays in whole animals regardless of the genetic endpoint examined (e.g., chromosome aberrations and SCEs in mouse bone marrow or gene mutations in transgenic mice) as well as the negative SCE results found in worker occupationally exposed to furfural. Overall, the data suggest that while furfural has intrinsic mutagenic potential in cultured mammalian cells, it is not expressed in whole animals since it is rapidly metabolized by the liver and rendered either non-mutagenic or markedly less mutagenic. Additionally, the negative data for the *in vivo* gene mutations assay, which examined the mouse liver as the target for furfural-induced tumorigenic activity, rule out mutagenicity as a possible mode of action for the induction of liver tumors seen in the 2-year mouse bioassay. Based on these considerations, there is no concern for mutagenicity.

B. Furfuryl Alcohol

The hydrogenated product of high pressure reduction of furfural, furfuryl alcohol was also assayed in a series of genetic toxicology studies sponsored by the NTP; summaries are presented below:

In Vitro Studies

Gene Mutation

The negative results of the NTP-sponsored *S. typhimurium* mammalian microsome mutagenicity assay conducted by Mortelmans *et al*. (1986) are discussed above with furfural.

Monien et al., (2011) found furfuryl alcohol to be mutagenic in *Salmonella typhimurium* TA100 strains engineered to express human sulfotransferase (TA100 SULT1A1*1 or TA100 SULT1A1*1Y), which is similar to the cytosolic protein level found in human liver (i.e., 0.3% or 2.6%, respectively). Additionally, the investigators found evidence of two DNA adducts [N^2-((furan-2-yl) methyl)-2' –deoxyguanosine (N^2-MFdG) and N^6-((furan-2-yl) methyl)-2' –deoxyadenosine (N^6-MFdA) in the bacterial DNA. Increases in revertant colonies were 2- and 4-fold higher than background for the strain showing the lower expression (TA100 SULT1A1*1) and 4- and 7-fold for the strain with the higher expression (TA100 SULT1A1*1Y) at 25 or 100 nmol/plate furfuryl alcohol, respectively. The investigators further reported that these findings correlated with the occurances of these adducts in the liver, lungs, and kidney of FVB/N mice receiving ≈390 mg/kg/day of furfuryl alcohol in drinking water for 28 days.

The findings of these investigation should be viewed with caution for several reasons: 1) there is little or no information on the bacterial strain characteristics, (*e.g.*, no historical control data); 2) the data should be confirmed in an independent study; 3) no primary data were presented; therefore, the presentation of means and standard errors instead of standard deviations for the bacterial mean values does not allow an independent assessment of variation around the means, 4) no primary data were presented for DNA adducts in the liver , kidney or lung of male mice, 5) findings of N^2-MFdG or N^6-MFdA adducts did not correlate with the induction of tumors at specific sites in the NTP mouse bioassay (e.g., similar levels of adducts were reported in the mouse liver, lung and kidney; however, the only site of tumor formation in the lifetime

inhalation bioassay mouse bioassay was the renal tubules. Furthermore, the dose at which adducts were detected was higher than the established maximum tolerated dose (60 mg/kg/day) and the tumorigenic dose for the NTP study. Based on these considerations, CARC concluded that these data do not provide reliable evidence of an *in vivo* genotoxic response.

Chromosome Aberrations

NTP also sponsored an *in vitro* mammalian cell chromosome aberration assay with furfuryl alcohol. In this study, Stich *et al.* (1981), exposed Chinese hamster ovary (CHO) cells to 0, 160, 300 or 500 µg/mL -S9 for 10 hours or 0, 300, 500 or 1000 µg/mL +S9 for 2 hours. Cultures were harvested at 12- 13 hours after treatment. Metaphase analysis revealed that in the absence of S9 activation, furfuryl alcohol was not clastogenic. With S9, the percentage of cells with chromosome aberrations was significantly ($p<0.05$) increased at 500 and 1000 µg/mL but the increase was not dose related or reproduced in a repeat trial.

Other Mutagenic Mechanisms

An *in vitro* investigation of sister chromatid exchanges (SCEs) in CHO cells was sponsored NTP and was conducted by Stich *et al*. (1981). In this study, CHO cells were exposed to 0, 16, 50, 160 or 500 µg/mL -S9 for 26 hours (Trial 1) or comparable non-activated concentrations for 26 hours (Trial 2) or 0, 16, 50, 160 or 500 µg/mL +S9 for 2 hours. Cells were processed and second division metaphases were analyzed. The non-activated test material at 500 µg/mL induced a positive increase in the percentage SCEs/chromosomes in Trial 1. This result was confirmed in Trial 2 with positive effects at 160 and 500 µg/mL -S9. By contrast, the S9-activated test material was not genotoxic.

The negative findings of the SCE study of Gomez-Arroyo and Souza (1985), with cultured human lymphocytes or lymphocytes collected from workers occupationally exposed to furfural or furfuryl alcohol, were previously discussed with furfural.

In Vivo Studies

In the NTP *in vivo* mouse bone marrow cytogenetic assays, furfuryl alcohol was not clastogenic in the bone marrow cells of male B6C3F1 mice harvested 17 hours after administration of 0, 75, 150 or 300 mg/kg by intrapertoneal injection. In bone marrow cells harvested at 36 hours after exposure to 0, 50, 100 or 200 mg/kg, no significant pairwise increases were observed but a significant ($p<0.05$) trend in cells with chromosome aberrations was seen. However, these results were not reproduced in two subsequent independent trials using comparable test material doses and a comparable harvest time. It was, therefore, concluded that furfuryl alcohol was not clastogenic in whole animals. A similar conclusion was drawn for the mouse bone marrow micronucleus assay performed with 6 groups of 5 male B6C3F1 mice dosed intraperitoneally with 0, 15.625, 31.25, 62.5, 125, or 250 mg/kg furfuryl alcohol/day for 3 consecutive days. Finally, furfuryl alcohol did not induce an increase in SCE in mouse bone marrow cells of male B6C3F1 mice receiving 0, 75, 150 or 300 mg/kg and sacrificed at 23 hours post-treatment or at 0, 37.5, 75 or 150 mg/kg and harvested at 23 hours post-treatment.

Overall Conclusions for Furfuryl Alcohol

Furfuryl alcohol has been studied in a battery of acceptable genetic toxicology assays, many of which were sponsored by the NTP, provided valuable information, and are acceptable for

regulatory purposes. The data indicate that furfuryl alcohol is not mutagenic in bacteria and does not cause chromosome aberrations or SCE induction in mammalian cells. These *in vitro* data are supported by the results of whole animals studies showing that furfuryl alcohol was not clastogenic, aneugenic or genotoxic in mouse bone marrow cytogenetic, micronucleus or SCE assays. It is, therefore, concluded that furfuryl alcohol does not present a mutagenic concern.

A.4.7 Neurotoxicity

870.6100 Delayed Neurotoxicity Study – Hen

Not Required

870.6200 Acute Neurotoxicity Screening Battery

In an acute neurotoxicity study (MRID 48998502; 48998501), groups of nonfasted, ~6-week-old Crl-CD(SD) rats (12/sex/dose) were given a single oral gavage dose of furfural (100% a.i., Lot # 20111216) in deionized water at doses of 0, 30, 80, or 200 mg/kg bw and observed for 14 days. Neurobehavioral assessment (functional observational battery (FOB) and motor activity testing) was performed in 12 animals/sex/group before dosing, one hour post dosing, and Days 7 and 14 post dosing. Cholinesterase activity was not determined. At study termination, 5 animals/sex/group were euthanized and perfused *in situ* for neuropathological examination. Of the perfused animals, 5 rats/sex each from the control and 200 mg/kg groups were subjected to histopathological evaluation of brain and peripheral nervous system tissues.

Treatment with 200 mg/kg of furfural produced multiple signs of toxicity including mortality, clinical signs, and changes in FOB parameters and motor activity that occurred only on the day of dosing (except for one mortality noted on Day 2). Five females and one male in the 200 mg/kg group did not survive to study termination (4 females and 1 male found dead or euthanized *in extremis* 4 to 7 hours following dosing; 1 female found dead 2 days post dosing). Adverse clinical signs were observed only in rats that died or were killed moribund, and included behavioral/CNS signs (prostrate position, lying on side, hunched, and hypoactivity), labored or decreased respiration, lacrimation, and salivation.

FOB changes were more pronounced in females compared to males and were present only on Day 0. Home cage and handling observations revealed that females had a higher incidence (9/12) of abnormal posture and slight lacrimation and salivation. Open-field observations of males revealed gait impairment, altered gait, and non-statistically increased time to first step. Females had increased ($p<0.05$) time to first step and in the number of animals with slight tremors, and decreased ($p<0.01$) mean number of rearing counts. Other changes included impaired mobility, resulting in fewer females with normal mobility compared to controls (0/12; $p<0.05$). Altered gait was noted in all females in the high-dose group and included statistically significant increases ($p<0.05$) in alterations such as dragging body with abdomen making contact, hindlimbs splayed or dragging, hunched body, or excessive ataxia, resulting in statistically fewer females with normal gait compared to controls (0/12; $p<0.05$). Slight but definite impairment in gait, considerable impairment in gait, marked impairment of gait, and severe impairment in gait were also observed in females, resulting in fewer high-dose females with normal gait (0/12; $p<0.05$). Arousal was adversely affected with only 3 females exhibiting normal arousal. Evaluation of sensory parameters revealed a lack of response to stimuli

(approach, touch, and/or startle response) in a few males, while females exhibited a lack of response to stimuli including approach, touch, startle, tail pinch, olfactory, and/or touch response to the eye. Additionally, a few females exhibited no forelimb extension, no hindlimb extension, and/or abnormal righting reflex. Neuromuscular observations revealed reduced hindlimb resistance, forelimb grip strength, and reduced rotarod performance in males (not statistically significant). Changes in females were more pronounced and attained statistical significance, and included no or reduced hindlimb resistance with only 2 females with normal hindlimb resistance, reduced forelimb and hindlimb grip strength (~40% of control values), reduced rotarod performance (5% of control), and reduced hindlimb foot splay (44% of control). Physiological observations revealed an increased catalepsy time observed in males (not significant) and females ($p \leq 0.01$), and reduced body temperature ($p \leq 0.01$) in females.

The registrant reported that both total and ambulatory motor activities were affected in high-dose males and females. Specifically, they found that within-session analyses of Day 0 revealed lower total motor activity counts during the first two subsessions (0-10 and 11-20 minutes) and in ambulatory motor activity counts during the first subsession (0-10 minutes). The decreases in activity were sufficient to result in a statistically significant ($p<0.05$) decrease in cumulative mean of total motor activity counts in females (-63% of control mean) and in the cumulative mean of ambulatory activity in both males (-35%) and females (-84%).

In an independent data analysis conducted by EPA using a different statistical approach, the females in the high (200 mg/kg) dose group showed both a significantly decreased daily cumulative total motor activity count (-61%) and a significantly decreased daily cumulative ambulatory motor activity count (-79%) on day 0. No significant treatment effects on the daily cumulative total and daily cumulative ambulatory motor activity counts were found in male animals.

EPA also performed an analysis to evaluate the treatment effects on habituation of the animals on each testing day. The high dose (200 mg/kg) showed a statistically significant difference in the habituation associated with total motor activity and ambulatory motor activity on day 0 in both males and females. The mid dose (80 mg/kg) showed a statistically significantly difference in the habituation of ambulatory activity in females only, on day 0. The registrant did not report any analysis of habituation.

Treatment with 200 mg/kg did not adversely affect body weight, gross or neuropathology findings, or brain weight. No other treatment-related effects were observed in males or females dosed with 30 or 80 mg/kg of furfural at any time point.

Based on the effects seen in this study, the Agency concluded that the LOAEL was 200 mg/kg bw/day (based on mortality and effects on FOB parameters and motor activity in males and females), with a NOAEL of 80 mg/kg bw/day.

This neurotoxicity study is classified as **acceptable/guideline** and satisfies the guideline requirement for an acute neurotoxicity study in rats (OCSPP 870.6200; OECD 424).

870.6200 Subchronic Neurotoxicity Screening Battery

Waived by HASPOC (TXR No. 0056939; D418688; 6/10/2014)

870.6300 Developmental Neurotoxicity Study

Not required.

A.4.8 Metabolism

870.7485 Metabolism - Rat

In a metabolism study (MRID 47750502) [^{14}C]-furfural radiolabelled in the carbonyl carbon (radiochemical purity 95%, batch/lot number not available) was administered to 4 male Fisher 344 rats per dose via gastric intubation. Doses were administered in corn oil (5 ml/kg) at dose levels of 0.127, 1.15, and 12.5 mg/kg. Radioactivity was quantified in urine and feces at intervals out to sacrifice at 72 hours, at which time radioactivity was also quantified in blood and tissues. A satellite group of 3 animals were administered furfural at 12.4 mg/kg, with radioactivity in exhaled air quantified out to 42 hours. Urinary metabolites were identified for the 0.127 and 12.5 mg/kg animals.

Overall recoveries were acceptable at 90% or above. Excretion data indicated that furfural was rapidly absorbed and eliminated at all dose levels, with about 80% elimination within 24hours.

The major route of elimination of furfural was excretion in the urine, in which 85% of the administered dose was found by 72 hours. There were no changes in excretion indicative of saturation of excretion with increasing dose. Expired radioactivity (as carbon dioxide) was a minor route of excretion at 6.6% and was measured for the high dose only. The feces were also a minor route of excretion at ≤2% of the administered dose. Furfural was retained in tissues at low levels of less than 1% of the administered dose (range 0.1 ± 0.1% at 0.127 mg/kg to 0.6 ± 0.1% at 12.5 mg/kg), indicating low potential for bioaccumulation.

Metabolites were identified and quantified only in the urine, as the urinary route was the only route of elimination (besides expired radioactivity at the high dose) for which metabolite levels exceeded 5%.

Furoylgylcine was the major urinary metabolite for both the high and low dose groups, comprising over 75% of urinary metabolites by 48 hours. Furoic acid and furanacrylic acid were minor urinary metabolites that were present at <5% after 48 hours. The average levels of unidentified urinary metabolites were low, at less than 2%.

These results support a metabolic pathway in which furfural is converted to furanacrylic acid (presumably by condensation with acetyl-CoA) which is excreted in the urine (a minor pathway) or oxidized to furoic acid (the major pathway). Furoic acid can be excreted unchanged in the urine (a minor pathway), decarboxylated and exhaled as carbon dioxide (a minor pathway), or conjugated with glycine to form furoylglycine, which is excreted in urine (the major pathway).

This metabolism study in rats and mice is classified **acceptable, non-guideline** and does not satisfy the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] because it was not conducted under GLP. However, it can be used to satisfy a data requirement for a metabolism study in rats and for other regulatory purposes.

870.7600 Dermal Absorption – Rat

None

A.4.9 Immunotoxicity

870.7800 Immunotoxicity

In an immunotoxicity study (MRID 48999301), furfural (100% a.i., Batch No. 20111216) was administered to 10 male Crl:CD(SD) rats/dose by oral gavage once daily for 28 consecutive days at dose levels of 0, 20, 40, 60, or 80 mg/kg bw/day. The immunological studies were divided into two parts. The first part consisted of the Spleen Antibody-Forming Cell Response (AFC Assay). The positive control group (10 rats) were administered 50 mg/kg bw/day of cyclophosphamide (CPS) via intraperitoneal injection once daily for 4 consecutive days before sacrifice. All rats in the AFC assay were immunized with a single 0.5 mL of 2 x 10^8 sheep red blood cells (sRBC) on study day 24. Following 28 days of exposure, rats were sacrificed and subjected to gross necropsy. The spleen, liver, and kidneys were weighed, and the spleen was processed for shipment to the laboratory conducting the immunological evaluations.

The second part consisted of the Natural Killer (NK) Assay. A group of positive control rats were administered 50 mg/kg bw/day of CPS via intraperitoneal injection once daily for 4 consecutive days before sacrifice (study days 24 through 27). In addition, another group of positive control rats were administered a single intravenous tail vein injection of 1.0 mL (1:10 dilution) of AAGM1 on study day 27, approximately 24 hours before euthanasia. At necropsy on Study Day 29, the liver, kidney, thymus and spleen weights were recorded, and the spleens were processed for shipment to the laboratory conducting the immunological evaluations. Peripheral Blood Phenotyping was also performed in the groups of rats in the NK groups. Blood samples were collected from nonfasted animals at necropsy. B and T lymphocytes, as well as monocytes, were quantitated using surface markers. The NK cell activity was evaluated with a ^{51}Cr release assay.

Treatment with up to 80 mg/kg/day of furfural did not adversely affect clinical signs, body weight, body weight gain, or food consumption. Gross necropsy did not reveal any treatment-related effects, and spleen and thymus weights were unaffected. One animal in the 60 mg/kg/day group died, but the death was not ascribed to treatment.

The systemic toxicity LOAEL could not be determined, and the NOAEL for systemic toxicity is ≥ 80 mg/kg/day.

AFC assay did not reveal statistically significant decreases in spleen cell number, specific activity (AFC/10^6 spleen cells) or total spleen activity (AFC/spleen) at any treated group compared to the control. High inter-individual variability was noted in all the treatment groups as well as in the control group. Evaluation of the individual animal data of this study did not show any trend or distribution that would demonstrate significant suppression of anti-SRBC AFC response. Animals in positive control group showed a statistically significant ($p< 0.01$) decrease of the anti-SRBC AFC response. This confirmed the ability of the test system to detect immuno-suppressive effects and confirmed the validity of the study design.

No changes in cell types were noted in animals treated with furfural when compared to animals in the control group as assessed with peripheral blood immunophenotyping. The CPS and AAGM1 positive control groups had statistically significant increases in absolute values of all examined cell types, but the percentage of each cell type was not affected.

NK cell activity assay did not reveal statistically significant changes at any treated group compared to the control indicated that furfural also did not suppress NK cell activity. The CPS and AAGM1 positive control groups exhibited statistically decreased NK cell activity at the three highest effector:target cell ratios.

The LOAEL for immunotoxicity could not be established, and the NOAEL for immunotoxicity is ≥ 80 mg/kg/day.

This immunotoxicity study is classified **acceptable/guideline** and satisfies the guideline requirement for an immunotoxicity study (OCSPP 870.7800) in rats.

APPENDIX B: Methodologies for Inhalation Risk Calculations and Human Equivalent Concentration Arrays

The Agency's approach used to calculate risks due to inhalation exposure (to furfural) is based on the guidance methodology developed by the Office of Research and Development (ORD) for the derivation of inhalation reference concentrations (RfCs) and human equivalent concentrations (HECs) for use in margin of exposure (MOE) calculations (RfC methodology). The RfC methodology applies a dosimetric adjustment that takes into consideration not only the differences in ventilation rate (MV) but also the physicochemical properties of the inhaled compound, the type of toxicity observed (*e.g.* systemic vs. port of entry) and the pharmacokinetic (PK) **but not pharmacodynamic** (PD) differences between animals and humans. Based on the RfC guidance (1994), the methodology for RfC derivation is an estimate of the quantitative dose-response assessment of chronic non-cancer toxicity for individual inhaled chemicals and includes dosimetric adjustment to account for the species-specific relationships of exposure concentration to deposited/delivered dose. This adjustment is influenced by the physicochemical properties of the inhaled compound as well as the type of toxicity observed (*e.g.* systemic vs. port of entry), and takes into consideration the PK differences between animals and humans. Though the RfC methodology was developed to estimate toxicity of inhaled chemicals over a lifetime, it can be used for other inhalation exposures (*e.g.* acute and short-term exposures) since the dosimetric adjustment incorporates mechanistic determinants of disposition that can be applied to shorter duration of exposures <u>provided the assumptions underlying the methodology are still valid</u>. These assumptions, in turn, vary depending on the type of toxicity observed and will be discussed later on in this document. Thus the derivation of a HEC for inhaled gases is described by the following equation:

$$HEC = POD_{study} * \frac{D_{\text{animal exposure (hrs / day)}}}{D_{\text{human exposure (hrs / day)}}} * \frac{W_{\text{animal exposure (days / wk)}}}{W_{\text{human exposure (days / wk)}}} * RGDR$$

Where:

POD_{study}: Point of departure identified in the critical toxicology study
$D_{animal\ exposure}$: Duration of animal exposure (hrs/day; days/wk)
$D_{anticipated\ exposure}$: Anticipated human duration of exposure (hrs/day; days/wk)
RGDR: Regional Gas Dose Ratio

For gases eliciting both port of entry and systemic effects, calculations to estimate the inhalation risk to humans are dependent on the regional gas dose ratio (RGDR). In the case of systemic effects, the RGDR is defined as the ratio of the blood:gas partition coefficient of the chemical for the test species to humans ($H_{b/g\ animal}/H_{b/g\ human}$). When this ratio is unknown or when the $H_{b/g\ animal} > H_{b/g\ human}$ a default value of 1.0 is used as the RGDR. This default is based on the observation that for chemicals where partition coefficient data are available in both rats and humans the RGDR value has usually been comparable or slightly higher than 1. Thus, the use of an RGDR of 1 results in a protective calculation of the inhalation risk. Some of the key assumptions fundamental to the use of the RfC methodology to derive a HEC based on systemic effects include:

1) all the concentrations of inhaled gas within the animal's body are periodic with respect to time (*i.e.* periodic steady state - the concentration *vs* time profile is the same for every week). Periodicity must be attained for at least 90% of the exposure.
2) in the respiratory tract, the air, tissue, capillary blood concentration are in equilibrium with respect to each other.
3) systemically, the blood and tissue concentrations are in equilibrium with respect to each other.

In the case of furfural, the physicochemical properties and metabolism data for the compound indicate that these conditions (*i.e.* periodicity and equilibrium between different compartments) will be achieved in a very short period of time. Under these conditions, therefore, the use of the RfC methodology to estimate acute inhalation risk is appropriate.

When the critical toxic effect in a study occurs in the respiratory tract (*i.e* port of entry effects), the RGDR is not related to the blood:gas partition coefficient of the compound but rather the ratio of the minute volume (MV) to the surface area (SA) of the affected region. In these instances, attaining periodicity or equilibrium between the compartments is not critical (since the effect is a function of the direct interaction between the inhaled compound and the affected region in the respiratory tract) and the RGDR may be calculated using the following equation:

$$RGDR = \frac{MV_{animal} / SA_{animal}}{MV_{human} / SA_{human}}$$

Where:

MV_{animal}: Minute volume for the test species (varies depending on body weight)
SA_{animal}: Surface area of the affected region in animals
MV_{human}: Minute volume for humans (default value is 13.8 l/min)
SA_{human}: Surface area of the affected region in humans

The MV_{animal} is calculated using the allometric scaling provided in USEPA (1988a). The equation for calculation of the MV_{animal} is:

$$\ln MV_{animal} = b_0 + b_1 \ln(BW)$$

Where:

$\ln MV_{animal}$: natural logarithm of the minute volume
b_0 : species specific intercept used in the algorithm to calculate minute volumes based on body weight
b_1: species specific coefficient used in the algorithm to calculate minute volumes based on body weight
ln BW: natural logarithm of the body weight (expressed in kg)

The values for the species-specific parameters used to calculate the MV_{animal} based on body weight and the values for the surface areas of various regions of the respiratory tract (extrathoracic, thoracic, and pulmonary) are provided in the EPA document "Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry" (1994).

The magnitude of the UFs applied when the RfC methodology is utilized takes into consideration the PK differences but not the PD differences. Consequently, the UF for interspecies extrapolation may be reduced to 3X (to account for the PD differences) while the UF for intraspecies variation is retained at 10X. Thus, the UF when using the RfC methodology is customarily 30X.

Appendix B/Table 1B: HC and HEC Array for Non-Occupational Risk Assessment[§]												
Relevant Study		**LOAEL (mg/m^3)**	**NOAEL (mg/m^3)**	**Da**	**Dh**	**Wa**	**Wh**	**RGDR**	**HEC (ppm)**	**inter**	**intra**	**UF**
Acute Exposure												
Acute inhalation- Rat (MRID 48563701)	Systemic	NA	NA	-	-	-	-	-	-	-	-	-
	ET	**NA**	**40**	**6**	**6**	**1**	**1**	**0.166**	**1.69**	**3**	**10**	**-**
Short-& Intermediate-Term Exposure												
28-day inhalation- Rat (MRID 47419101)	Systemic	NA	NA	-	-	-	-	-	-	-	-	-
	ET	**20**	**8**	**6**	**6**	**5**	**7**	**0.166**	**0.24**	**3**	**10**	**-**
Long Term Exposure: Not appropriate for furfural												

[§] Bolded studies used for endpoint selection.

Key for Array Tables	
LOAEL: Lowest observed adverse effect level *Da*: Daily animal exposure (hrs/day) *Wa*: Weekly animal exposure (days/week) *RGDR*: Regional Gas Dose Ratio *inter*: interspecies extrapolation uncertainty factor	*Dh*: Anticipated daily human exposure (hrs/day) *Wh*: Anticipated weekly human exposure (days/week) *HC:* Human Concentration *HEC*: Human Equivalent Concentration *intra*: intraspecies variation uncertainty factor *UF*: Other uncertainty factor(s)

Appendix B/Table 2B: HC and HEC Array for Occupational Risk Assessment[§]												
Relevant Study		**LOAEL (mg/m^3)**	**NOAEL (mg/m^3)**	**Da**	**Dh**	**Wa**	**Wh**	**RGDR**	**HEC (ppm)**	**inter**	**intra**	**UF**
Acute Exposure												
Acute inhalation- Rat (MRID 48563701)	Systemic	NA	NA	-	-	-	-	NA	NA	-	-	-
	ET	**NA**	**40**	**6**	**6**	**1**	**1**	**0.166**	**1.69**	**3**	**10**	**-**
Short- and Intermediate-Term Exposure												
28-day inhalation- Rat (MRID 47419101)	Systemic	NA	NA	-	-	-	-	NA	NA	-	-	-
	ET	**20**	**8**	**6**	**6**	**5**	**5**	**0.166**	**0.34**	**3**	**10**	**-**
Long Term Exposure: Not appropriate for furfural												

[§] Bolded studies used for endpoint selection.

Key for Array Tables	
LOAEL: Lowest observed adverse effect level *Da*: Daily animal exposure (hrs/day) *Wa*: Weekly animal exposure (days/week) *RGDR*: Regional Gas Dose Ratio *inter*: interspecies extrapolation uncertainty factor	*Dh*: Anticipated daily human exposure (hrs/day) *Wh*: Anticipated weekly human exposure (days/week) *HC:* Human Concentration *HEC*: Human Equivalent Concentration *intra*: intraspecies variation uncertainty factor *UF*: Other uncertainty factor(s)

APPENDIX C: PERFUM Output Description

PERFUM works by establishing a grid with receptor points around a field built with spokes and rings (see Figure C1). PERFUM then calculates air concentrations at each receptor location on this grid for each day of meteorological data in each analysis (5 years of weather data were used in this assessment). Air concentrations are calculated at each grid location which are in turn, used to calculate distances in each array where the COC is reached. PERFUM compiles these results for each array (or spoke) then ultimately compiles them across all spokes and weather days using two techniques (i.e., referred to as a "whole field" or "maximum" buffer).

Whole field buffer results are calculated using PERFUM by compiling the results for all arrays (i.e., using the entire perimeter) of each day's contour line outputs. PERFUM compiles all of the locations (i.e., x and y coordinates) along the contours in each of the plots into one distribution and essentially produces an overall contour plot for the 5 years of weather data (see Figure C2 below). The user can then select a percentile of the distribution of interest (e.g., 95th percentile or 99th percentile). In essence, the "whole field" buffer results represent the entire range of possible exposures regardless of location relative to the treated field.

Maximum buffer results from PERFUM are calculated by compiling only the farthest distances from the contours produced for each weather day. PERFUM also generates these maximum distance buffers across 5 years of weather data which is presented in Figure 4.2 below. The user can then select a percentile of the distribution of interest (e.g., 95th percentile or 99th percentile). In summary, the maximum buffer results can be thought of as a way of providing more resolution around the upper percentiles of possible exposure. In a physical sense, it can also possibly be applicable to individuals who live in an area with strong prevailing winds due to topography or other factors (e.g., in a valley or coastal situation where on-shore winds are predominant).

Figure C1: PERFUM Receptor Grid

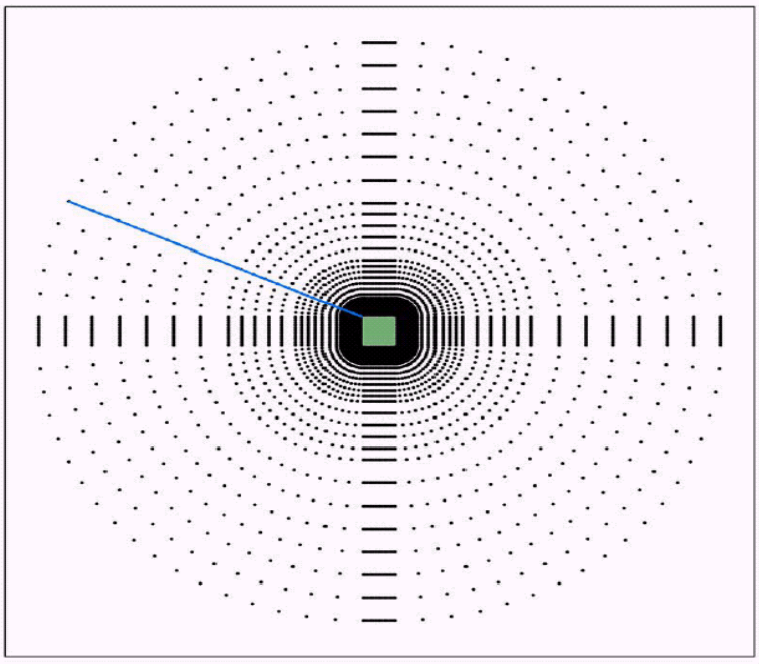
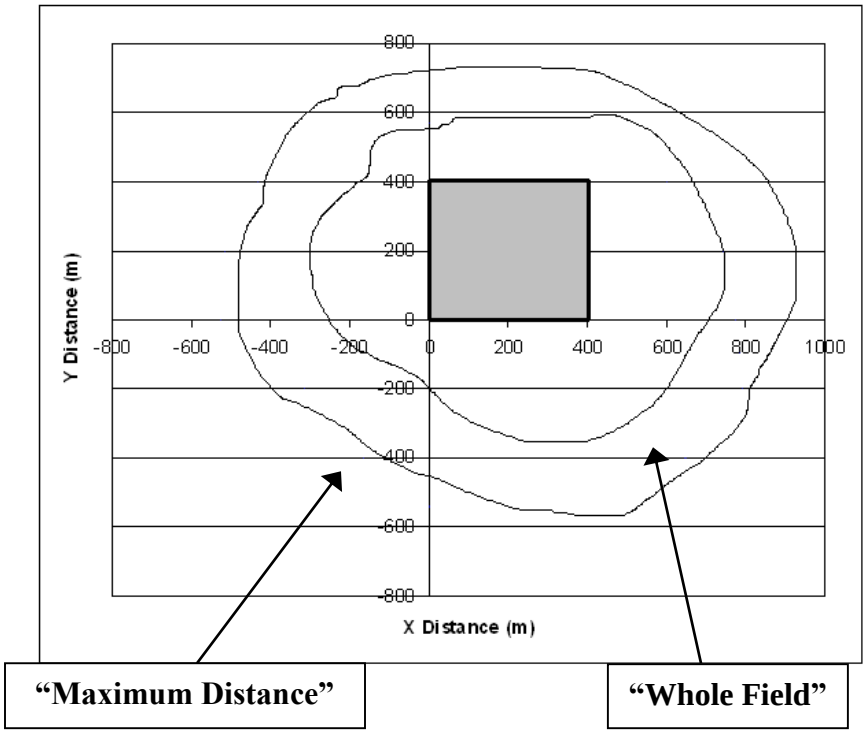


Figure C2: Whole Field vs. Maximum Buffer Distance Example



PERFUM can generate the types of outputs discussed above for different exposure periods. An averaging time of 6 hours was used for both bystander and occupational exposure because flux measurements dropped to negligible levels within this period. This timeframe also matches the duration of the acute inhalation toxicity study on which the COC is based. The maximum concentration and whole field distributional results from PERFUM can be described as follows:

> The **maximum concentration** distribution at the 95th percentile provides a buffer zone whereby there will not be an exceedance for 95% of the days. A 95th percentile buffer zone using the maximum concentration distribution will result in the modeled air concentrations exceeding the COC somewhere around the perimeter in 5 out of every 100 applications.
>
> For the **whole field** distribution, the 95th percentile whole field buffer distance is that distance below which all buffer distances, from all spokes, on all days will fall. A 95th percentile buffer zone using the whole field distribution will result in air concentrations that will not exceed the COC along 95% of the total combined buffer zone perimeters for all 100 applications. This does not mean that whole field buffer zones are protective along the buffer zone perimeter in 95% of applications. Therefore, whole field buffer zones do not provide any defined level of protection for individual applications.

APPENDIX D:Flux Profiles from Field Volatility Studies

The flux profiles for Field 3 in the Florida turf volatility study and Field 1 from the tomato farm bare soil volatility study are provided below.

Table D1. Estimated Furfural Fluxes for Field 3 – Turf Farm				
Period	**Sample Interval Time**	**Start Time**	**Duration (hh:mm)**	**Registrant Estimated Flux (µg/m²-s)**
1A	03/01/2010 08:00-10:30	3/1/10 8:00	2.30	117.80
1B	03/01/2010 10:30-13:00	3/1/10 10:30	2.30	0.40
1C	03/01/2010 13:00-15:30	3/1/10 13:00	2.30	0.40
2	03/01/2010 1500 - 2000	3/1/10 15:00	5:00	0.01
3	03/01/2010 2000 - 0130	3/1/10 20:00	5:30	0.01
4	03/02/2010 0130 - 0800	3/2/10 1:30	6:30	0.01
5	03/02/2010 0800 - 1415	3/2/10 8:00	6:15	0.03
6	03/02/2010 1415 - 1945	3/2/10 14:15	5:30	0.04
7	03/02/2010 1945 - 0115	3/2/10 19:45	5:30	0.03
8	03/03/2010 0115 - 0745	3/3/10 1:15	6:30	0.02
9	03/03/2010 0745 - 1915	3/3/10 7:45	11:30	0.03
10	03/03/2010 1915 - 0715	3/3/10 19:15	12:00	
11	03/04/2010 0715 - 1915	3/4/10 7:15		

Table D2. Estimated Furfural Fluxes for Field 1 – Tomato Farm – Bare Soil				
Period	**Sample Start Time**	**Sample End Time**	**Duration (hh:mm)**	**Registrant Estimated Flux (µg/m²-s)**
1A	3/14/2011 10:30	3/14/2011 15:30	5.0	5.43
1C	3/14/2011 15:30	3/14/2011 18:00	2.5	1.41
2	3/14/2011 18:00	3/14/2011 19:00	1.0	0.01
3	3/14/2011 19:00	3/15/2011 1:00	6.0	0.31
4	3/15/2011 1:00	3/15/2011 7:00	6.0	0.09
5	3/15/2011 7:00	3/15/2011 13:00	6.0	0.02
6	3/15/2011 13:00	3/15/2011 19:00	6.0	0.16
7	3/15/2011 19:00	3/16/2011 1:00	6.0	0.13
8	3/16/2011 1:00	3/16/2011 7:00	6.0	0.05
9	3/16/2011 7:00	3/16/2011 19:00	12.0	0.05
10	3/16/2011 19:00	3/17/2011 7:00	12.0	0.03
11	3/17/2011 7:00	3/17/2011 19:00	12.0	0.01

APPENDIX E: Air Concentrations (µg/m3) at Varied Distances from Treated Fields (1 to 40 Acres)

Table E1. Air Concentrations (µg/m^3) at Varied Distances from a 1-Acre Treated Field[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	2	2	2	2	2	2	2	2	2	--
	60	2	2	2	2	2	2	2	2	2	2
	70	98	82	58	28	12	2	2	2	2	2
	75	152	138	112	78	52	18	2	2	2	2
	80	202	192	172	138	108	62	18	2	2	2
	85	248	238	222	192	168	118	58	32	22	18
	90	298	292	282	258	228	182	118	78	62	52
	95	388	382	378	358	332	282	202	148	128	112
Bakersfield	50	2	2	2	2	2	2	2	2	2	--
	60	2	2	2	2	2	2	2	2	2	2
	70	98	82	58	28	12	2	2	2	2	2
	75	152	138	112	78	52	18	2	2	2	2
	80	202	192	172	138	108	62	18	2	2	2
	85	248	238	222	192	168	118	58	32	22	18
	90	298	292	282	258	228	182	118	78	62	52
	95	388	382	378	358	332	282	202	148	128	112
Bradenton	50	2	2	2	2	2	2	2	--	--	--
	60	2	2	2	2	2	2	2	2	2	2
	70	82	62	42	18	8	2	2	2	2	2
	75	158	138	112	72	48	18	2	2	2	2
	80	238	222	192	152	118	68	22	8	2	2
	85	318	302	278	238	198	138	68	38	28	18
	90	408	398	372	328	288	218	132	82	68	58
	95	528	518	498	448	402	322	212	152	132	112
Flint	50	2	2	2	2	2	--	--	--	--	--
	60	2	2	2	2	2	2	2	2	--	--
	70	72	62	48	28	12	2	2	2	2	2
	75	118	108	92	68	52	22	2	2	2	2
	80	162	152	142	118	98	62	22	8	2	2
	85	198	192	188	168	142	108	62	38	28	22
	90	248	242	232	212	192	152	102	68	58	48
	95	318	318	308	288	268	222	158	112	98	88
Tallahassee	50	2	2	2	2	2	2	2	--	--	--
	60	2	2	2	2	2	2	2	2	2	2
	70	72	58	38	18	8	2	2	2	2	2
	75	128	118	98	68	42	12	2	2	2	2
	80	178	168	152	128	102	62	18	2	2	2
	85	228	218	208	182	158	118	62	32	22	18
	90	278	278	262	242	218	178	112	78	68	52
	95	358	352	342	322	302	258	188	138	122	108
Yakima	50	8	2	2	2	2	2	2	2	2	2
	60	62	48	32	12	8	2	2	2	2	2
	70	122	112	98	72	52	28	2	2	2	2
	75	152	142	128	102	82	52	18	8	2	2
	80	188	178	162	138	118	82	42	22	18	12
	85	222	218	202	178	152	118	72	42	38	28
	90	272	262	248	222	198	158	108	72	62	52
	95	338	332	322	302	278	228	162	118	102	92

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

-- indicates concentration estimate is zero for this percentile at this distance.

Table E2. Air Concentrations (µg/m^3) at Varied Distances from a 3-Acre Treated Field[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	2	2	2	2	2	2	2	2	2	2
	60	38	22	12	2	2	2	2	2	2	2
	70	192	172	142	102	72	28	2	2	2	2
	75	262	242	218	172	138	88	28	8	2	2
	80	322	308	288	248	212	152	82	42	28	18
	85	392	378	358	322	288	228	148	98	82	68
	90	482	472	452	418	382	318	228	172	152	132
	95	633	628	608	578	542	472	368	292	262	238
Bakersfield	50	2	2	2	2	2	2	2	2	2	2
	60	38	22	12	2	2	2	2	2	2	2
	70	192	172	142	102	72	28	2	2	2	2
	75	262	242	218	172	138	88	28	8	2	2
	80	322	308	288	248	212	152	82	42	28	18
	85	392	378	358	322	288	228	148	98	82	68
	90	482	472	452	418	382	318	228	172	152	132
	95	633	628	608	578	542	472	368	292	262	238
Bradenton	50	2	2	2	2	2	2	2	2	2	2
	60	18	12	2	2	2	2	2	2	2	2
	70	182	158	128	82	52	22	2	2	2	2
	75	282	258	228	178	138	82	28	8	2	2
	80	382	362	332	282	238	172	88	42	32	22
	85	482	468	438	392	342	268	168	108	88	72
	90	608	592	568	512	462	372	262	188	162	138
	95	778	762	738	678	622	522	382	292	258	232
Flint	50	2	2	2	2	2	2	--	--	--	--
	60	28	18	8	2	2	2	2	2	2	2
	70	148	138	118	88	62	32	2	2	2	2
	75	212	198	182	152	128	82	32	12	8	2
	80	268	258	242	212	188	142	82	48	38	28
	85	322	312	298	272	248	202	138	98	82	68
	90	392	382	372	342	318	268	192	148	128	112
	95	518	508	492	462	428	368	278	218	198	178
Tallahassee	50	2	2	2	2	2	2	2	2	2	2
	60	22	12	8	2	2	2	2	2	2	2
	70	158	142	118	82	52	18	2	2	2	2
	75	232	218	192	158	128	78	22	2	2	2
	80	302	288	268	232	202	152	82	42	32	22
	85	372	362	342	312	282	228	152	102	88	72
	90	452	448	432	402	368	308	228	172	152	132
	95	578	568	553	518	488	428	328	268	238	218
Yakima	50	32	22	12	2	2	2	2	2	2	2
	60	122	108	88	58	38	12	2	2	2	2
	70	208	192	172	142	118	78	32	12	8	2
	75	248	238	218	188	158	118	68	38	28	22
	80	298	282	262	232	202	158	102	68	58	48
	85	352	338	318	288	258	208	142	102	92	78
	90	428	412	392	358	328	272	198	148	132	118
	95	538	522	508	478	442	382	288	228	202	188

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

-- indicates concentration estimate is zero for this percentile at this distance.

Table E3. Air Concentrations (µg/m³) at Varied Distances from a 5-Acre Treated Field[1]											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	2	2	2	2	2	2	2	2	2	2
	60	50	36	22	10	2	2	2	2	2	2
	70	168	154	132	102	78	44	10	2	2	2
	75	220	208	188	158	132	92	44	16	10	6
	80	268	256	240	212	188	144	88	54	40	30
	85	324	316	298	270	242	202	140	102	84	76
	90	400	394	378	352	324	274	206	160	144	130
	95	528	522	508	484	456	404	322	264	240	220
Bakersfield	50	2	2	2	2	2	2	2	2	2	2
	60	48	36	28	14	6	2	2	2	2	2
	70	164	154	140	116	96	64	28	6	2	2
	75	220	212	194	172	146	110	64	36	28	16
	80	274	268	254	226	202	160	106	68	54	44
	85	338	330	316	288	260	216	150	110	92	82
	90	414	404	390	364	336	284	208	160	140	124
	95	524	514	500	470	442	384	294	232	212	194
Bradenton	50	2	2	2	2	2	2	2	2	2	2
	60	28	20	10	2	2	2	2	2	2	2
	70	164	146	126	92	64	34	6	2	2	2
	75	242	226	202	168	136	92	40	16	10	6
	80	316	302	282	246	216	160	96	58	44	34
	85	394	384	364	324	294	236	160	112	96	82
	90	490	480	460	422	384	318	232	178	154	136
	95	624	614	592	552	510	436	332	264	236	212
Flint	50	2	2	2	2	2	2	2	--	--	--
	60	36	28	20	10	2	2	2	2	2	2
	70	132	124	110	88	68	40	14	2	2	2
	75	180	172	160	140	120	84	44	22	16	10
	80	222	216	206	184	168	132	84	58	48	36
	85	268	260	250	228	212	178	126	96	82	72
	90	324	318	308	288	268	226	172	132	120	110
	95	426	418	408	384	360	316	242	194	178	160
Tallahassee	50	2	2	2	2	2	2	2	2	2	2
	60	30	22	14	2	2	2	2	2	2	2
	70	144	132	112	88	64	34	6	2	2	2
	75	202	188	174	146	124	88	40	16	10	6
	80	256	246	228	206	180	144	88	58	44	36
	85	312	302	288	264	242	202	144	106	92	78
	90	378	370	360	338	316	270	202	158	140	126
	95	480	470	460	436	408	364	284	232	212	198
Yakima	50	36	28	20	10	2	2	2	2	2	2
	60	110	98	82	62	44	22	2	2	2	2
	70	174	164	150	126	106	78	44	22	16	10
	75	208	198	184	160	140	110	68	44	36	30
	80	246	236	222	198	174	144	98	72	62	50
	85	288	282	268	242	220	180	132	98	88	78
	90	350	342	330	302	274	232	174	136	124	112
	95	442	432	418	394	370	322	254	206	184	168

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.

-- indicates concentration estimate is zero for this percentile at this distance.

Table E4. Air Concentrations (µg/m³) at Varied Distances from a 10-Acre Treated Field[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	2	2	2	2	2	2	2	2	2	2
	60	98	82	62	36	20	6	2	2	2	2
	70	226	212	188	158	130	88	36	14	6	2
	75	282	270	250	220	188	144	84	50	36	28
	80	338	324	308	276	250	206	140	98	82	68
	85	412	398	378	350	318	270	202	158	140	124
	90	510	500	484	452	422	366	284	228	208	192
	95	668	662	644	618	586	530	432	364	336	312
Bakersfield	50	2	2	2	2	2	2	2	2	2	2
	60	92	82	68	44	30	10	2	2	2	2
	70	222	212	194	172	146	110	62	34	22	16
	75	284	274	256	228	206	164	106	72	58	48
	80	350	338	322	294	268	222	158	112	98	84
	85	426	414	400	370	338	288	212	164	144	126
	90	514	504	486	456	426	370	288	226	206	184
	95	648	638	620	590	558	498	400	324	294	270
Bradenton	50	2	2	2	2	2	2	2	2	2	2
	60	64	50	34	16	10	2	2	2	2	2
	70	232	216	188	154	124	78	30	10	6	2
	75	318	302	274	236	206	154	88	48	36	28
	80	400	386	364	324	290	236	158	110	92	76
	85	490	476	456	414	380	318	232	174	154	136
	90	600	586	566	524	484	414	316	250	226	206
	95	754	744	720	676	632	552	438	360	324	302
Flint	50	2	2	2	2	2	2	2	2	2	0
	60	72	62	48	30	16	6	2	2	2	2
	70	184	174	160	136	116	82	40	16	10	6
	75	236	226	212	192	172	132	84	54	44	34
	80	282	274	264	242	222	184	132	98	84	72
	85	336	330	316	294	274	236	180	144	126	112
	90	408	400	386	364	338	298	232	188	172	158
	95	534	528	514	486	460	408	330	270	250	228
Tallahassee	50	2	2	2	2	2	2	2	2	2	2
	60	68	54	36	20	10	2	2	2	2	2
	70	202	188	172	140	116	78	30	10	6	2
	75	264	254	236	208	180	140	84	50	36	28
	80	324	318	302	274	246	206	144	102	88	76
	85	398	386	370	342	316	274	206	160	144	130
	90	476	470	456	428	404	356	282	226	206	192
	95	604	592	578	548	522	470	384	318	294	274
Yakima	50	68	58	44	28	14	2	2	2	2	2
	60	146	136	120	96	78	50	20	6	2	2
	70	222	212	194	172	150	116	76	48	40	30
	75	264	254	240	212	188	154	106	76	64	58
	80	312	298	282	256	232	194	144	110	96	84
	85	364	352	336	308	284	242	184	146	132	120
	90	438	428	414	384	356	308	240	194	178	160
	95	558	548	530	504	476	422	338	284	264	242

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.

Table E5. Air Concentrations (µg/m^3) at Varied Distances from a 40-Acre Treated Field[1]

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6
	60	15.6	15.6	10.4	10.4	10.4	2.6	2.6	2.6	2.6	2.6
	70	28.6	28.6	23.4	23.4	15.6	15.6	10.4	2.6	2.6	2.6
	75	36.4	28.6	28.6	23.4	23.4	15.6	10.4	10.4	10.4	2.6
	80	36.4	36.4	36.4	28.6	28.6	23.4	15.6	10.4	10.4	10.4
	85	41.6	41.6	36.4	36.4	28.6	28.6	23.4	15.6	15.6	15.6
	90	41.6	41.6	41.6	36.4	36.4	28.6	23.4	23.4	23.4	15.6
	95	49.4	49.4	41.6	41.6	41.6	36.4	28.6	28.6	23.4	23.4
Bakersfield	50	10.4	10.4	10.4	10.4	2.6	2.6	2.6	2.6	2.6	2.6
	60	23.4	23.4	23.4	15.6	15.6	10.4	10.4	2.6	2.6	2.6
	70	36.4	36.4	28.6	28.6	23.4	23.4	15.6	10.4	10.4	10.4
	75	41.6	41.6	36.4	36.4	28.6	23.4	15.6	15.6	10.4	10.4
	80	49.4	49.4	41.6	41.6	36.4	28.6	23.4	15.6	15.6	15.6
	85	54.6	54.6	49.4	49.4	41.6	36.4	28.6	23.4	23.4	15.6
	90	62.4	62.4	54.6	54.6	49.4	41.6	36.4	28.6	28.6	23.4
	95	75.4	75.4	67.6	62.4	62.4	54.6	41.6	36.4	36.4	28.6
Bradenton	50	10.4	10.4	10.4	10.4	2.6	2.6	2.6	2.6	2.6	2.6
	60	23.4	23.4	23.4	15.6	15.6	10.4	10.4	2.6	2.6	2.6
	70	36.4	36.4	28.6	28.6	23.4	23.4	15.6	10.4	10.4	10.4
	75	41.6	41.6	36.4	36.4	28.6	23.4	15.6	15.6	10.4	10.4
	80	49.4	49.4	41.6	41.6	36.4	28.6	23.4	15.6	15.6	15.6
	85	54.6	54.6	49.4	49.4	41.6	36.4	28.6	23.4	23.4	15.6
	90	62.4	62.4	54.6	54.6	49.4	41.6	36.4	28.6	28.6	23.4
	95	75.4	75.4	67.6	62.4	62.4	54.6	41.6	36.4	36.4	28.6
Flint	50	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6
	60	15.6	15.6	10.4	10.4	10.4	2.6	2.6	2.6	2.6	2.6
	70	23.4	23.4	23.4	23.4	15.6	15.6	10.4	10.4	2.6	2.6
	75	28.6	28.6	28.6	28.6	23.4	23.4	15.6	10.4	10.4	10.4
	80	36.4	36.4	36.4	28.6	28.6	23.4	15.6	15.6	15.6	10.4
	85	41.6	41.6	36.4	36.4	36.4	28.6	23.4	23.4	15.6	15.6
	90	49.4	49.4	41.6	41.6	41.6	36.4	28.6	23.4	23.4	23.4
	95	54.6	54.6	54.6	49.4	49.4	41.6	36.4	28.6	28.6	28.6
Tallahassee	50	10.4	10.4	10.4	2.6	2.6	2.6	2.6	2.6	2.6	2.6
	60	15.6	15.6	15.6	15.6	10.4	10.4	2.6	2.6	2.6	2.6
	70	28.6	28.6	23.4	23.4	15.6	15.6	10.4	10.4	10.4	2.6
	75	28.6	28.6	28.6	23.4	23.4	15.6	15.6	10.4	10.4	10.4
	80	36.4	36.4	36.4	28.6	28.6	23.4	15.6	15.6	10.4	10.4
	85	41.6	41.6	36.4	36.4	36.4	28.6	23.4	15.6	15.6	15.6
	90	49.4	49.4	41.6	41.6	36.4	36.4	28.6	23.4	23.4	15.6
	95	54.6	54.6	54.6	49.4	49.4	41.6	36.4	28.6	28.6	28.6
Yakima	50	15.6	15.6	15.6	10.4	10.4	10.4	2.6	2.6	2.6	2.6
	60	23.4	23.4	23.4	15.6	15.6	15.6	10.4	2.6	2.6	2.6
	70	28.6	28.6	28.6	23.4	23.4	15.6	15.6	10.4	10.4	10.4
	75	36.4	36.4	36.4	28.6	28.6	23.4	15.6	15.6	10.4	10.4
	80	41.6	41.6	36.4	36.4	28.6	28.6	23.4	15.6	15.6	15.6
	85	49.4	49.4	41.6	41.6	36.4	28.6	23.4	23.4	15.6	15.6
	90	54.6	54.6	54.6	49.4	41.6	41.6	28.6	28.6	23.4	23.4
	95	75.4	75.4	67.6	67.6	62.4	54.6	41.6	36.4	36.4	28.6

[1] Based on 6-hour average whole field PERFUM run estimated from the Florida tomato farm (bare soil) Field 1 flux profile, with an application rate of 390 lb ai/A. Values presented reflect the total air concentration (i.e., furfural plus furfuryl alcohol) as furfuryl alcohol was found to occur as a soil degradate (up to 30% of parent) when furfural is applied to bare ground.

APPENDIX F: 10- and 5-Year Amortized Cancer Risk Estimates at Varied Distances from Treated Fields (1 to 40 Acres)

Table F1. Cancer Risk Estimates for Varied Distances from a 1-Acre Treated Field – Turf (Golf Course)[1] 10-yr Exposure

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	0.0E+00
	60	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	5.2E-06	4.3E-06	3.1E-06	1.5E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	8.0E-06	7.3E-06	5.9E-06	4.1E-06	2.7E-06	9.5E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	80	1.1E-05	1.0E-05	9.1E-06	7.3E-06	5.7E-06	3.3E-06	9.5E-07	1.1E-07	1.1E-07	1.1E-07
	85	1.3E-05	1.3E-05	1.2E-05	1.0E-05	8.8E-06	6.2E-06	3.1E-06	1.7E-06	1.2E-06	9.5E-07
	90	1.6E-05	1.5E-05	1.5E-05	1.4E-05	1.2E-05	9.6E-06	6.2E-06	4.1E-06	3.3E-06	2.7E-06
Bakersfield	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	5.2E-06	4.6E-06	3.8E-06	2.5E-06	1.5E-06	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	8.0E-06	7.5E-06	6.7E-06	5.2E-06	4.1E-06	2.2E-06	4.2E-07	1.1E-07	1.1E-07	1.1E-07
	80	1.1E-05	1.0E-05	9.6E-06	8.0E-06	6.7E-06	4.6E-06	2.0E-06	6.3E-07	4.2E-07	1.1E-07
	85	1.4E-05	1.3E-05	1.3E-05	1.1E-05	9.6E-06	7.3E-06	3.8E-06	2.2E-06	1.7E-06	1.2E-06
	90	1.7E-05	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.0E-05	6.4E-06	4.1E-06	3.3E-06	2.7E-06
Bradenton	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	0.0E+00	0.0E+00	0.0E+00
	60	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	4.3E-06	3.3E-06	2.2E-06	9.5E-07	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	8.3E-06	7.3E-06	5.9E-06	3.8E-06	2.5E-06	9.5E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	80	1.3E-05	1.2E-05	1.0E-05	8.0E-06	6.2E-06	3.6E-06	1.2E-06	4.2E-07	1.1E-07	1.1E-07
	85	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.0E-05	7.3E-06	3.6E-06	2.0E-06	1.5E-06	9.5E-07
	90	2.1E-05	2.1E-05	2.0E-05	1.7E-05	1.5E-05	1.1E-05	6.9E-06	4.3E-06	3.6E-06	3.1E-06
Flint	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	0.0E+00	0.0E+00	0.0E+00	0.0E+00	0.0E+00
	60	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	0.0E+00	0.0E+00
	70	3.8E-06	3.3E-06	2.5E-06	1.5E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	6.2E-06	5.7E-06	4.8E-06	3.6E-06	2.7E-06	1.2E-06	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	80	8.5E-06	8.0E-06	7.5E-06	6.2E-06	5.2E-06	3.3E-06	1.2E-06	4.2E-07	1.1E-07	1.1E-07
	85	1.0E-05	1.0E-05	9.9E-06	8.8E-06	7.5E-06	5.7E-06	3.3E-06	2.0E-06	1.5E-06	1.2E-06
	90	1.3E-05	1.3E-05	1.2E-05	1.1E-05	1.0E-05	8.0E-06	5.4E-06	3.6E-06	3.1E-06	2.5E-06
Tallahassee	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	0.0E+00	0.0E+00	0.0E+00
	60	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	3.8E-06	3.1E-06	2.0E-06	9.5E-07	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	6.7E-06	6.2E-06	5.2E-06	3.6E-06	2.2E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	80	9.4E-06	8.8E-06	8.0E-06	6.7E-06	5.4E-06	3.3E-06	9.5E-07	1.1E-07	1.1E-07	1.1E-07
	85	1.2E-05	1.1E-05	1.1E-05	9.6E-06	8.3E-06	6.2E-06	3.3E-06	1.7E-06	1.2E-06	9.5E-07
	90	1.5E-05	1.5E-05	1.4E-05	1.3E-05	1.1E-05	9.4E-06	5.9E-06	4.1E-06	3.6E-06	2.7E-06
Yakima	50	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	3.3E-06	2.5E-06	1.7E-06	6.3E-07	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	6.4E-06	5.9E-06	5.2E-06	3.8E-06	2.7E-06	1.5E-06	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	8.0E-06	7.5E-06	6.7E-06	5.4E-06	4.3E-06	2.7E-06	9.5E-07	4.2E-07	1.1E-07	1.1E-07
	80	9.9E-06	9.4E-06	8.5E-06	7.3E-06	6.2E-06	4.3E-06	2.2E-06	1.2E-06	9.5E-07	6.3E-07
	85	1.2E-05	1.1E-05	1.1E-05	9.4E-06	8.0E-06	6.2E-06	3.8E-06	2.2E-06	2.0E-06	1.5E-06
	90	1.4E-05	1.4E-05	1.3E-05	1.2E-05	1.0E-05	8.3E-06	5.7E-06	3.8E-06	3.3E-06	2.7E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\,-1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(6 application days/365-day year) x (10 years exposed/78-yr lifetime).

-- indicates concentration estimate is zero for this percentile at this distance.

Highlighted column indicates buffer zone proposed on label for this use.

Table F2. Cancer Risk Estimates for Varied Distances from a 3-Acre Treated Field – Turf (Athletic Field/Sod)[1] 10-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	2.0E-06	1.2E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.0E-05	9.1E-06	7.5E-06	5.4E-06	3.8E-06	1.5E-06	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	1.4E-05	1.3E-05	1.1E-05	9.1E-06	7.3E-06	4.6E-06	1.5E-06	4.2E-07	1.1E-07	1.1E-07
	80	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.1E-05	8.0E-06	4.3E-06	2.2E-06	1.5E-06	9.5E-07
	85	2.1E-05	2.0E-05	1.9E-05	1.7E-05	1.5E-05	1.2E-05	7.8E-06	5.2E-06	4.3E-06	3.6E-06
	90	2.5E-05	2.5E-05	2.4E-05	2.2E-05	2.0E-05	1.7E-05	1.2E-05	9.1E-06	8.0E-06	6.9E-06
Bakersfield	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	1.7E-06	1.2E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	9.9E-06	9.1E-06	8.0E-06	6.4E-06	4.8E-06	3.1E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07
	75	1.4E-05	1.3E-05	1.2E-05	1.0E-05	8.5E-06	5.9E-06	3.1E-06	1.2E-06	6.3E-07	4.2E-07
	80	1.7E-05	1.7E-05	1.6E-05	1.4E-05	1.2E-05	9.4E-06	5.4E-06	3.3E-06	2.5E-06	2.0E-06
	85	2.2E-05	2.1E-05	2.0E-05	1.8E-05	1.6E-05	1.3E-05	8.5E-06	5.9E-06	4.8E-06	4.1E-06
	90	2.6E-05	2.6E-05	2.5E-05	2.3E-05	2.1E-05	1.7E-05	1.2E-05	9.1E-06	7.8E-06	6.7E-06
Bradenton	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	9.5E-07	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	9.6E-06	8.3E-06	6.7E-06	4.3E-06	2.7E-06	1.2E-06	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	1.5E-05	1.4E-05	1.2E-05	9.4E-06	7.3E-06	4.3E-06	1.5E-06	4.2E-07	1.1E-07	1.1E-07
	80	2.0E-05	1.9E-05	1.7E-05	1.5E-05	1.3E-05	9.1E-06	4.6E-06	2.2E-06	1.7E-06	1.2E-06
	85	2.5E-05	2.5E-05	2.3E-05	2.1E-05	1.8E-05	1.4E-05	8.8E-06	5.7E-06	4.6E-06	3.8E-06
	90	3.2E-05	3.1E-05	3.0E-05	2.7E-05	2.4E-05	2.0E-05	1.4E-05	9.9E-06	8.5E-06	7.3E-06
Flint	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	0.0E+00	0.0E+00	0.0E+00	0.0E+00
	60	1.5E-06	9.5E-07	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	7.8E-06	7.3E-06	6.2E-06	4.6E-06	3.3E-06	1.7E-06	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	1.1E-05	1.0E-05	9.6E-06	8.0E-06	6.7E-06	4.3E-06	1.7E-06	6.3E-07	4.2E-07	1.1E-07
	80	1.4E-05	1.4E-05	1.3E-05	1.1E-05	9.9E-06	7.5E-06	4.3E-06	2.5E-06	2.0E-06	1.5E-06
	85	1.7E-05	1.6E-05	1.6E-05	1.4E-05	1.3E-05	1.1E-05	7.3E-06	5.2E-06	4.3E-06	3.6E-06
	90	2.1E-05	2.0E-05	2.0E-05	1.8E-05	1.7E-05	1.4E-05	1.0E-05	7.8E-06	6.7E-06	5.9E-06
Tallahassee	50	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	1.2E-06	6.3E-07	4.2E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	8.3E-06	7.5E-06	6.2E-06	4.3E-06	2.7E-06	9.5E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	75	1.2E-05	1.1E-05	1.0E-05	8.3E-06	6.7E-06	4.1E-06	1.2E-06	1.1E-07	1.1E-07	1.1E-07
	80	1.6E-05	1.5E-05	1.4E-05	1.2E-05	1.1E-05	8.0E-06	4.3E-06	2.2E-06	1.7E-06	1.2E-06
	85	2.0E-05	1.9E-05	1.8E-05	1.6E-05	1.5E-05	1.2E-05	8.0E-06	5.4E-06	4.6E-06	3.8E-06
	90	2.4E-05	2.4E-05	2.3E-05	2.1E-05	1.9E-05	1.6E-05	1.2E-05	9.1E-06	8.0E-06	6.9E-06
Yakima	50	1.7E-06	1.2E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	60	6.4E-06	5.7E-06	4.6E-06	3.1E-06	2.0E-06	6.3E-07	1.1E-07	1.1E-07	1.1E-07	1.1E-07
	70	1.1E-05	1.0E-05	9.1E-06	7.5E-06	6.2E-06	4.1E-06	1.7E-06	6.3E-07	4.2E-07	1.1E-07
	75	1.3E-05	1.3E-05	1.1E-05	9.9E-06	8.3E-06	6.2E-06	3.6E-06	2.0E-06	1.5E-06	1.2E-06
	80	1.6E-05	1.5E-05	1.4E-05	1.2E-05	1.1E-05	8.3E-06	5.4E-06	3.6E-06	3.1E-06	2.5E-06
	85	1.9E-05	1.8E-05	1.7E-05	1.5E-05	1.4E-05	1.1E-05	7.5E-06	5.4E-06	4.8E-06	4.1E-06
	90	2.3E-05	2.2E-05	2.1E-05	1.9E-05	1.7E-05	1.4E-05	1.0E-05	7.8E-06	6.9E-06	6.2E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\,-1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(6 application days/365-day year) x (10 years exposed/78-yr lifetime).

-- indicates concentration estimate is zero for this percentile at this distance.

Highlighted column indicates buffer zone proposed on label for this use.

Table F3. Cancer Risk Estimates for Varied Distances from a 5-Acre Treated Field – Ornamentals[1] 10-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	3.5E-06	2.5E-06	1.5E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.2E-05	1.1E-05	9.3E-06	7.2E-06	5.5E-06	3.1E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07
	75	1.5E-05	1.5E-05	1.3E-05	1.1E-05	9.3E-06	6.5E-06	3.1E-06	1.1E-06	7.0E-07	4.2E-07
	80	1.9E-05	1.8E-05	1.7E-05	1.5E-05	1.3E-05	1.0E-05	6.2E-06	3.8E-06	2.8E-06	2.1E-06
	85	2.3E-05	2.2E-05	2.1E-05	1.9E-05	1.7E-05	1.4E-05	9.8E-06	7.2E-06	5.9E-06	5.3E-06
	90	2.8E-05	2.8E-05	2.7E-05	2.5E-05	2.3E-05	1.9E-05	1.4E-05	1.1E-05	1.0E-05	9.1E-06
Bakersfield	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	3.4E-06	2.5E-06	2.0E-06	9.8E-07	4.2E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.2E-05	1.1E-05	9.8E-06	8.1E-06	6.7E-06	4.5E-06	2.0E-06	4.2E-07	1.4E-07	1.4E-07
	75	1.5E-05	1.5E-05	1.4E-05	1.2E-05	1.0E-05	7.7E-06	4.5E-06	2.5E-06	2.0E-06	1.1E-06
	80	1.9E-05	1.9E-05	1.8E-05	1.6E-05	1.4E-05	1.1E-05	7.4E-06	4.8E-06	3.8E-06	3.1E-06
	85	2.4E-05	2.3E-05	2.2E-05	2.0E-05	1.8E-05	1.5E-05	1.1E-05	7.7E-06	6.5E-06	5.8E-06
	90	2.9E-05	2.8E-05	2.7E-05	2.6E-05	2.4E-05	2.0E-05	1.5E-05	1.1E-05	9.8E-06	8.7E-06
Bradenton	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	2.0E-06	1.4E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.2E-05	1.0E-05	8.8E-06	6.5E-06	4.5E-06	2.4E-06	4.2E-07	1.4E-07	1.4E-07	1.4E-07
	75	1.7E-05	1.6E-05	1.4E-05	1.2E-05	9.5E-06	6.5E-06	2.8E-06	1.1E-06	7.0E-07	4.2E-07
	80	2.2E-05	2.1E-05	2.0E-05	1.7E-05	1.5E-05	1.1E-05	6.7E-06	4.1E-06	3.1E-06	2.4E-06
	85	2.8E-05	2.7E-05	2.6E-05	2.3E-05	2.1E-05	1.7E-05	1.1E-05	7.9E-06	6.7E-06	5.8E-06
	90	3.4E-05	3.4E-05	3.2E-05	3.0E-05	2.7E-05	2.2E-05	1.6E-05	1.2E-05	1.1E-05	9.5E-06
Flint	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	0.0E+00	0.0E+00	0.0E+00
	60	2.5E-06	2.0E-06	1.4E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	9.3E-06	8.7E-06	7.7E-06	6.2E-06	4.8E-06	2.8E-06	9.8E-07	1.4E-07	1.4E-07	1.4E-07
	75	1.3E-05	1.2E-05	1.1E-05	9.8E-06	8.4E-06	5.9E-06	3.1E-06	1.5E-06	1.1E-06	7.0E-07
	80	1.6E-05	1.5E-05	1.4E-05	1.3E-05	1.2E-05	9.3E-06	5.9E-06	4.1E-06	3.4E-06	2.5E-06
	85	1.9E-05	1.8E-05	1.8E-05	1.6E-05	1.5E-05	1.2E-05	8.8E-06	6.7E-06	5.8E-06	5.1E-06
	90	2.3E-05	2.2E-05	2.2E-05	2.0E-05	1.9E-05	1.6E-05	1.2E-05	9.3E-06	8.4E-06	7.7E-06
Tallahassee	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	2.1E-06	1.5E-06	9.8E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.0E-05	9.3E-06	7.9E-06	6.2E-06	4.5E-06	2.4E-06	4.2E-07	1.4E-07	1.4E-07	1.4E-07
	75	1.4E-05	1.3E-05	1.2E-05	1.0E-05	8.7E-06	6.2E-06	2.8E-06	1.1E-06	7.0E-07	4.2E-07
	80	1.8E-05	1.7E-05	1.6E-05	1.4E-05	1.3E-05	1.0E-05	6.2E-06	4.1E-06	3.1E-06	2.5E-06
	85	2.2E-05	2.1E-05	2.0E-05	1.9E-05	1.7E-05	1.4E-05	1.0E-05	7.4E-06	6.5E-06	5.5E-06
	90	2.7E-05	2.6E-05	2.5E-05	2.4E-05	2.2E-05	1.9E-05	1.4E-05	1.1E-05	9.8E-06	8.8E-06
Yakima	50	2.5E-06	2.0E-06	1.4E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	7.7E-06	6.9E-06	5.8E-06	4.4E-06	3.1E-06	1.5E-06	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.2E-05	1.2E-05	1.1E-05	8.8E-06	7.4E-06	5.5E-06	3.1E-06	1.5E-06	1.1E-06	7.0E-07
	75	1.5E-05	1.4E-05	1.3E-05	1.1E-05	9.8E-06	7.7E-06	4.8E-06	3.1E-06	2.5E-06	2.1E-06
	80	1.7E-05	1.7E-05	1.6E-05	1.4E-05	1.2E-05	1.0E-05	6.9E-06	5.1E-06	4.4E-06	3.5E-06
	85	2.0E-05	2.0E-05	1.9E-05	1.7E-05	1.5E-05	1.3E-05	9.3E-06	6.9E-06	6.2E-06	5.5E-06
	90	2.5E-05	2.4E-05	2.3E-05	2.1E-05	1.9E-05	1.6E-05	1.2E-05	9.5E-06	8.7E-06	7.9E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.

Cancer Risk Estimate = Q* (2.5 x 10-5 $\mu g/m^{3\,-1}$) x Air concentration at a given distance ($\mu g/m^3$; see Appendix E) x Amortization factors [(8 application days/365-day year) x (10 years exposed/78-yr lifetime).

Highlighted column indicates buffer zone proposed on label for this use.

Table F4. Cancer Risk Estimates for Varied Distances from a 10-Acre Treated Field - Ornamentals[1] 10-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	6.9E-06	5.8E-06	4.4E-06	2.5E-06	1.4E-06	4.2E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.6E-05	1.5E-05	1.3E-05	1.1E-05	9.1E-06	6.2E-06	2.5E-06	9.8E-07	4.2E-07	1.4E-07
	75	2.0E-05	1.9E-05	1.8E-05	1.5E-05	1.3E-05	1.0E-05	5.9E-06	3.5E-06	2.5E-06	2.0E-06
	80	2.4E-05	2.3E-05	2.2E-05	1.9E-05	1.8E-05	1.4E-05	9.8E-06	6.9E-06	5.8E-06	4.8E-06
	85	2.9E-05	2.8E-05	2.7E-05	2.5E-05	2.2E-05	1.9E-05	1.4E-05	1.1E-05	9.8E-06	8.7E-06
	90	3.6E-05	3.5E-05	3.4E-05	3.2E-05	3.0E-05	2.6E-05	2.0E-05	1.6E-05	1.5E-05	1.3E-05
Bakersfield	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	6.5E-06	5.8E-06	4.8E-06	3.1E-06	2.1E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.6E-05	1.5E-05	1.4E-05	1.2E-05	1.0E-05	7.7E-06	4.4E-06	2.4E-06	1.5E-06	1.1E-06
	75	2.0E-05	1.9E-05	1.8E-05	1.6E-05	1.4E-05	1.2E-05	7.4E-06	5.1E-06	4.1E-06	3.4E-06
	80	2.5E-05	2.4E-05	2.3E-05	2.1E-05	1.9E-05	1.6E-05	1.1E-05	7.9E-06	6.9E-06	5.9E-06
	85	3.0E-05	2.9E-05	2.8E-05	2.6E-05	2.4E-05	2.0E-05	1.5E-05	1.2E-05	1.0E-05	8.8E-06
	90	3.6E-05	3.5E-05	3.4E-05	3.2E-05	3.0E-05	2.6E-05	2.0E-05	1.6E-05	1.4E-05	1.3E-05
Bradenton	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	4.5E-06	3.5E-06	2.4E-06	1.1E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.6E-05	1.5E-05	1.3E-05	1.1E-05	8.7E-06	5.5E-06	2.1E-06	7.0E-07	4.2E-07	1.4E-07
	75	2.2E-05	2.1E-05	1.9E-05	1.7E-05	1.4E-05	1.1E-05	6.2E-06	3.4E-06	2.5E-06	2.0E-06
	80	2.8E-05	2.7E-05	2.6E-05	2.3E-05	2.0E-05	1.7E-05	1.1E-05	7.7E-06	6.5E-06	5.3E-06
	85	3.4E-05	3.3E-05	3.2E-05	2.9E-05	2.7E-05	2.2E-05	1.6E-05	1.2E-05	1.1E-05	9.5E-06
	90	4.2E-05	4.1E-05	4.0E-05	3.7E-05	3.4E-05	2.9E-05	2.2E-05	1.8E-05	1.6E-05	1.4E-05
Flint	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	0.0E+00
	60	5.1E-06	4.4E-06	3.4E-06	2.1E-06	1.1E-06	4.2E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.3E-05	1.2E-05	1.1E-05	9.5E-06	8.1E-06	5.8E-06	2.8E-06	1.1E-06	7.0E-07	4.2E-07
	75	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.2E-05	9.3E-06	5.9E-06	3.8E-06	3.1E-06	2.4E-06
	80	2.0E-05	1.9E-05	1.9E-05	1.7E-05	1.6E-05	1.3E-05	9.3E-06	6.9E-06	5.9E-06	5.1E-06
	85	2.4E-05	2.3E-05	2.2E-05	2.1E-05	1.9E-05	1.7E-05	1.3E-05	1.0E-05	8.8E-06	7.9E-06
	90	2.9E-05	2.8E-05	2.7E-05	2.6E-05	2.4E-05	2.1E-05	1.6E-05	1.3E-05	1.2E-05	1.1E-05
Tallahassee	50	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	4.8E-06	3.8E-06	2.5E-06	1.4E-06	7.0E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	70	1.4E-05	1.3E-05	1.2E-05	9.8E-06	8.1E-06	5.5E-06	2.1E-06	7.0E-07	4.2E-07	1.4E-07
	75	1.9E-05	1.8E-05	1.7E-05	1.5E-05	1.3E-05	9.8E-06	5.9E-06	3.5E-06	2.5E-06	2.0E-06
	80	2.3E-05	2.2E-05	2.1E-05	1.9E-05	1.7E-05	1.4E-05	1.0E-05	7.2E-06	6.2E-06	5.3E-06
	85	2.8E-05	2.7E-05	2.6E-05	2.4E-05	2.2E-05	1.9E-05	1.4E-05	1.1E-05	1.0E-05	9.1E-06
	90	3.3E-05	3.3E-05	3.2E-05	3.0E-05	2.8E-05	2.5E-05	2.0E-05	1.6E-05	1.4E-05	1.3E-05
Yakima	50	4.8E-06	4.1E-06	3.1E-06	2.0E-06	9.8E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07	1.4E-07
	60	1.0E-05	9.5E-06	8.4E-06	6.7E-06	5.5E-06	3.5E-06	1.4E-06	4.2E-07	1.4E-07	1.4E-07
	70	1.6E-05	1.5E-05	1.4E-05	1.2E-05	1.1E-05	8.1E-06	5.3E-06	3.4E-06	2.8E-06	2.1E-06
	75	1.9E-05	1.8E-05	1.7E-05	1.5E-05	1.3E-05	1.1E-05	7.4E-06	5.3E-06	4.5E-06	4.1E-06
	80	2.2E-05	2.1E-05	2.0E-05	1.8E-05	1.6E-05	1.4E-05	1.0E-05	7.7E-06	6.7E-06	5.9E-06
	85	2.6E-05	2.5E-05	2.4E-05	2.2E-05	2.0E-05	1.7E-05	1.3E-05	1.0E-05	9.3E-06	8.4E-06
	90	3.1E-05	3.0E-05	2.9E-05	2.7E-05	2.5E-05	2.2E-05	1.7E-05	1.4E-05	1.2E-05	1.1E-05

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.
Cancer Risk Estimate = Q* (2.5 x 10-5 $\mu g/m^{3\,-1}$) x Air concentration at a given distance ($\mu g/m^3$; see Appendix E) x Amortization factors [(8 application days/365-day year) x (10 years exposed/78-yr lifetime).
Highlighted column indicates buffer zone proposed on label for this use.

Table F5. Cancer Risk Estimates for Varied Distances from a 40-Acre Treated Field – Bare Soil[1] 5-yr Exposure

Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	60	6.8E-08	6.8E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	70	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08
	75	1.6E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08
	80	1.6E-07	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	6.8E-08	4.6E-08	4.6E-08	4.6E-08
	85	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08
	90	1.8E-07	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	1.0E-07	6.8E-08
Bakersfield	50	4.6E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	60	1.0E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08
	70	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	4.6E-08	4.6E-08	4.6E-08
	75	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08
	80	2.2E-07	2.2E-07	1.8E-07	1.8E-07	1.6E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08
	85	2.4E-07	2.4E-07	2.2E-07	2.2E-07	1.8E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08
	90	2.7E-07	2.7E-07	2.4E-07	2.4E-07	2.2E-07	1.8E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07
Bradenton	50	4.6E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	60	1.0E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08
	70	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	4.6E-08	4.6E-08	4.6E-08
	75	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08
	80	2.2E-07	2.2E-07	1.8E-07	1.8E-07	1.6E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08
	85	2.4E-07	2.4E-07	2.2E-07	2.2E-07	1.8E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08
	90	2.7E-07	2.7E-07	2.4E-07	2.4E-07	2.2E-07	1.8E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07
Flint	50	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	60	6.8E-08	6.8E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	70	1.0E-07	1.0E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08
	75	1.3E-07	1.3E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	4.6E-08	4.6E-08	4.6E-08
	80	1.6E-07	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08	4.6E-08
	85	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08
	90	2.2E-07	2.2E-07	1.8E-07	1.8E-07	1.8E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	1.0E-07
Tallahassee	50	4.6E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	60	6.8E-08	6.8E-08	6.8E-08	6.8E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	70	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08
	75	1.3E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08	4.6E-08
	80	1.6E-07	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08
	85	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.6E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08
	90	2.2E-07	2.2E-07	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08
Yakima	50	6.8E-08	6.8E-08	6.8E-08	4.6E-08	4.6E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08	1.1E-08
	60	1.0E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08	4.6E-08	1.1E-08	1.1E-08	1.1E-08
	70	1.3E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08	4.6E-08
	75	1.6E-07	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	4.6E-08	4.6E-08
	80	1.8E-07	1.8E-07	1.6E-07	1.6E-07	1.3E-07	1.3E-07	1.0E-07	6.8E-08	6.8E-08	6.8E-08
	85	2.2E-07	2.2E-07	1.8E-07	1.8E-07	1.6E-07	1.3E-07	1.0E-07	1.0E-07	6.8E-08	6.8E-08
	90	2.4E-07	2.4E-07	2.4E-07	2.2E-07	1.8E-07	1.8E-07	1.3E-07	1.3E-07	1.0E-07	1.0E-07

[1] Based on 6-hour average whole field PERFUM run estimated from the Florida tomato farm (bare soil) Field 1 flux profile, with an application rate of 390 lb ai/A. Values presented reflect the total air concentration (i.e., furfural plus furfuryl alcohol) as furfuryl alcohol was found to occur as a soil degradate (up to 30% of parent) when furfural is applied to bare ground.

Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\,-1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(1 application day/365-day year) x (5 years exposed/78-yr lifetime).

Highlighted column indicates buffer zone proposed on label for this use.

Table F6. Cancer Risk Estimates for Varied Distances from a 1-Acre Treated Field – Turf (Golf Course)[1] 5-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	**50**	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	0.0E+00
	60	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	2.6E-06	2.2E-06	1.5E-06	7.4E-07	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	4.0E-06	3.6E-06	2.9E-06	2.1E-06	1.4E-06	4.7E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	80	5.3E-06	5.1E-06	4.5E-06	3.6E-06	2.8E-06	1.6E-06	4.7E-07	5.3E-08	5.3E-08	5.3E-08
	85	6.5E-06	6.3E-06	5.8E-06	5.1E-06	4.4E-06	3.1E-06	1.5E-06	8.4E-07	5.8E-07	4.7E-07
	90	7.8E-06	7.7E-06	7.4E-06	6.8E-06	6.0E-06	4.8E-06	3.1E-06	2.1E-06	1.6E-06	1.4E-06
Bakersfield	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	2.6E-06	2.3E-06	1.9E-06	1.3E-06	7.4E-07	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	4.0E-06	3.7E-06	3.4E-06	2.6E-06	2.1E-06	1.1E-06	2.1E-07	5.3E-08	5.3E-08	5.3E-08
	80	5.3E-06	5.2E-06	4.8E-06	4.0E-06	3.4E-06	2.3E-06	1.0E-06	3.2E-07	2.1E-07	5.3E-08
	85	6.8E-06	6.6E-06	6.3E-06	5.5E-06	4.8E-06	3.6E-06	1.9E-06	1.1E-06	8.4E-07	5.8E-07
	90	8.5E-06	8.4E-06	7.9E-06	7.3E-06	6.4E-06	5.1E-06	3.2E-06	2.1E-06	1.6E-06	1.4E-06
Bradenton	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	0.0E+00	0.0E+00	0.0E+00
	60	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	2.2E-06	1.6E-06	1.1E-06	4.7E-07	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	4.2E-06	3.6E-06	2.9E-06	1.9E-06	1.3E-06	4.7E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	80	6.3E-06	5.8E-06	5.1E-06	4.0E-06	3.1E-06	1.8E-06	5.8E-07	2.1E-07	5.3E-08	5.3E-08
	85	8.4E-06	7.9E-06	7.3E-06	6.3E-06	5.2E-06	3.6E-06	1.8E-06	1.0E-06	7.4E-07	4.7E-07
	90	1.1E-05	1.0E-05	9.8E-06	8.6E-06	7.6E-06	5.7E-06	3.5E-06	2.2E-06	1.8E-06	1.5E-06
Flint	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	0.0E+00	0.0E+00	0.0E+00	0.0E+00	0.0E+00
	60	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	0.0E+00	0.0E+00
	70	1.9E-06	1.6E-06	1.3E-06	7.4E-07	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	3.1E-06	2.8E-06	2.4E-06	1.8E-06	1.4E-06	5.8E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	80	4.3E-06	4.0E-06	3.7E-06	3.1E-06	2.6E-06	1.6E-06	5.8E-07	2.1E-07	5.3E-08	5.3E-08
	85	5.2E-06	5.1E-06	4.9E-06	4.4E-06	3.7E-06	2.8E-06	1.6E-06	1.0E-06	7.4E-07	5.8E-07
	90	6.5E-06	6.4E-06	6.1E-06	5.6E-06	5.1E-06	4.0E-06	2.7E-06	1.8E-06	1.5E-06	1.3E-06
Tallahassee	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	0.0E+00	0.0E+00	0.0E+00
	60	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	1.9E-06	1.5E-06	1.0E-06	4.7E-07	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	3.4E-06	3.1E-06	2.6E-06	1.8E-06	1.1E-06	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	80	4.7E-06	4.4E-06	4.0E-06	3.4E-06	2.7E-06	1.6E-06	4.7E-07	5.3E-08	5.3E-08	5.3E-08
	85	6.0E-06	5.7E-06	5.5E-06	4.8E-06	4.2E-06	3.1E-06	1.6E-06	8.4E-07	5.8E-07	4.7E-07
	90	7.3E-06	7.3E-06	6.9E-06	6.4E-06	5.7E-06	4.7E-06	2.9E-06	2.1E-06	1.8E-06	1.4E-06
Yakima	50	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	1.6E-06	1.3E-06	8.4E-07	3.2E-07	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	3.2E-06	2.9E-06	2.6E-06	1.9E-06	1.4E-06	7.4E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	4.0E-06	3.7E-06	3.4E-06	2.7E-06	2.2E-06	1.4E-06	4.7E-07	2.1E-07	5.3E-08	5.3E-08
	80	4.9E-06	4.7E-06	4.3E-06	3.6E-06	3.1E-06	2.2E-06	1.1E-06	5.8E-07	4.7E-07	3.2E-07
	85	5.8E-06	5.7E-06	5.3E-06	4.7E-06	4.0E-06	3.1E-06	1.9E-06	1.1E-06	1.0E-06	7.4E-07
	90	7.2E-06	6.9E-06	6.5E-06	5.8E-06	5.2E-06	4.2E-06	2.8E-06	1.9E-06	1.6E-06	1.4E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\,-1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(6 application days/365-day year) x (5 years exposed/78-yr lifetime).

-- indicates concentration estimate is zero for this percentile at this distance.

Highlighted column indicates buffer zone proposed on label for this use.

Table F7. Cancer Risk Estimates for Varied Distances from a 3-Acre Treated Field – Turf (Athletic Field/Sod)[1] 5-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	1.0E-06	5.8E-07	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	5.1E-06	4.5E-06	3.7E-06	2.7E-06	1.9E-06	7.4E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	6.9E-06	6.4E-06	5.7E-06	4.5E-06	3.6E-06	2.3E-06	7.4E-07	2.1E-07	5.3E-08	5.3E-08
	80	8.5E-06	8.1E-06	7.6E-06	6.5E-06	5.6E-06	4.0E-06	2.2E-06	1.1E-06	7.4E-07	4.7E-07
	85	1.0E-05	9.9E-06	9.4E-06	8.5E-06	7.6E-06	6.0E-06	3.9E-06	2.6E-06	2.2E-06	1.8E-06
	90	1.3E-05	1.2E-05	1.2E-05	1.1E-05	1.0E-05	8.4E-06	6.0E-06	4.5E-06	4.0E-06	3.5E-06
Bakersfield	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	8.4E-07	5.8E-07	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	4.9E-06	4.5E-06	4.0E-06	3.2E-06	2.4E-06	1.5E-06	3.2E-07	5.3E-08	5.3E-08	5.3E-08
	75	6.9E-06	6.5E-06	6.0E-06	5.1E-06	4.3E-06	2.9E-06	1.5E-06	5.8E-07	3.2E-07	2.1E-07
	80	8.7E-06	8.4E-06	7.8E-06	6.9E-06	6.1E-06	4.7E-06	2.7E-06	1.6E-06	1.3E-06	1.0E-06
	85	1.1E-05	1.0E-05	9.9E-06	9.0E-06	8.1E-06	6.5E-06	4.3E-06	2.9E-06	2.4E-06	2.1E-06
	90	1.3E-05	1.3E-05	1.3E-05	1.2E-05	1.1E-05	8.7E-06	6.1E-06	4.5E-06	3.9E-06	3.4E-06
Bradenton	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	4.7E-07	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	4.8E-06	4.2E-06	3.4E-06	2.2E-06	1.4E-06	5.8E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	7.4E-06	6.8E-06	6.0E-06	4.7E-06	3.6E-06	2.2E-06	7.4E-07	2.1E-07	5.3E-08	5.3E-08
	80	1.0E-05	9.5E-06	8.7E-06	7.4E-06	6.3E-06	4.5E-06	2.3E-06	1.1E-06	8.4E-07	5.8E-07
	85	1.3E-05	1.2E-05	1.2E-05	1.0E-05	9.0E-06	7.1E-06	4.4E-06	2.8E-06	2.3E-06	1.9E-06
	90	1.6E-05	1.6E-05	1.5E-05	1.3E-05	1.2E-05	9.8E-06	6.9E-06	4.9E-06	4.3E-06	3.6E-06
Flint	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	0.0E+00	0.0E+00	0.0E+00	0.0E+00
	60	7.4E-07	4.7E-07	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	3.9E-06	3.6E-06	3.1E-06	2.3E-06	1.6E-06	8.4E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	5.6E-06	5.2E-06	4.8E-06	4.0E-06	3.4E-06	2.2E-06	8.4E-07	3.2E-07	2.1E-07	5.3E-08
	80	7.1E-06	6.8E-06	6.4E-06	5.6E-06	4.9E-06	3.7E-06	2.2E-06	1.3E-06	1.0E-06	7.4E-07
	85	8.5E-06	8.2E-06	7.8E-06	7.2E-06	6.5E-06	5.3E-06	3.6E-06	2.6E-06	2.2E-06	1.8E-06
	90	1.0E-05	1.0E-05	9.8E-06	9.0E-06	8.4E-06	7.1E-06	5.1E-06	3.9E-06	3.4E-06	2.9E-06
Tallahassee	50	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	5.8E-07	3.2E-07	2.1E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	4.2E-06	3.7E-06	3.1E-06	2.2E-06	1.4E-06	4.7E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	75	6.1E-06	5.7E-06	5.1E-06	4.2E-06	3.4E-06	2.1E-06	5.8E-07	5.3E-08	5.3E-08	5.3E-08
	80	7.9E-06	7.6E-06	7.1E-06	6.1E-06	5.3E-06	4.0E-06	2.2E-06	1.1E-06	8.4E-07	5.8E-07
	85	9.8E-06	9.5E-06	9.0E-06	8.2E-06	7.4E-06	6.0E-06	4.0E-06	2.7E-06	2.3E-06	1.9E-06
	90	1.2E-05	1.2E-05	1.1E-05	1.1E-05	9.7E-06	8.1E-06	6.0E-06	4.5E-06	4.0E-06	3.5E-06
Yakima	50	8.4E-07	5.8E-07	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	60	3.2E-06	2.8E-06	2.3E-06	1.5E-06	1.0E-06	3.2E-07	5.3E-08	5.3E-08	5.3E-08	5.3E-08
	70	5.5E-06	5.1E-06	4.5E-06	3.7E-06	3.1E-06	2.1E-06	8.4E-07	3.2E-07	2.1E-07	5.3E-08
	75	6.5E-06	6.3E-06	5.7E-06	4.9E-06	4.2E-06	3.1E-06	1.8E-06	1.0E-06	7.4E-07	5.8E-07
	80	7.8E-06	7.4E-06	6.9E-06	6.1E-06	5.3E-06	4.2E-06	2.7E-06	1.8E-06	1.5E-06	1.3E-06
	85	9.3E-06	8.9E-06	8.4E-06	7.6E-06	6.8E-06	5.5E-06	3.7E-06	2.7E-06	2.4E-06	2.1E-06
	90	1.1E-05	1.1E-05	1.0E-05	9.4E-06	8.6E-06	7.2E-06	5.2E-06	3.9E-06	3.5E-06	3.1E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A.

Cancer Risk Estimate = Q* (2.5 x 10-5 µg/m$^{3\,-1}$) x Air concentration at a given distance (µg/m^3; see Appendix E) x Amortization factors [(6 application days/365-day year) x (5 years exposed/78-yr lifetime).

-- indicates concentration estimate is zero for this percentile at this distance.

Highlighted column indicates buffer zone proposed on label for this use.

Table F8. Cancer Risk Estimates for Varied Distances from a 5-Acre Treated Field – Ornamentals[1] 5-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	1.8E-06	1.3E-06	7.7E-07	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	5.9E-06	5.4E-06	4.6E-06	3.6E-06	2.7E-06	1.5E-06	3.5E-07	7.0E-08	7.0E-08	7.0E-08
	75	7.7E-06	7.3E-06	6.6E-06	5.5E-06	4.6E-06	3.2E-06	1.5E-06	5.6E-07	3.5E-07	2.1E-07
	80	9.4E-06	9.0E-06	8.4E-06	7.4E-06	6.6E-06	5.1E-06	3.1E-06	1.9E-06	1.4E-06	1.1E-06
	85	1.1E-05	1.1E-05	1.0E-05	9.5E-06	8.5E-06	7.1E-06	4.9E-06	3.6E-06	2.9E-06	2.7E-06
	90	1.4E-05	1.4E-05	1.3E-05	1.2E-05	1.1E-05	9.6E-06	7.2E-06	5.6E-06	5.1E-06	4.6E-06
Bakersfield	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	1.7E-06	1.3E-06	9.8E-07	4.9E-07	2.1E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	5.8E-06	5.4E-06	4.9E-06	4.1E-06	3.4E-06	2.2E-06	9.8E-07	2.1E-07	7.0E-08	7.0E-08
	75	7.7E-06	7.4E-06	6.8E-06	6.0E-06	5.1E-06	3.9E-06	2.2E-06	1.3E-06	9.8E-07	5.6E-07
	80	9.6E-06	9.4E-06	8.9E-06	7.9E-06	7.1E-06	5.6E-06	3.7E-06	2.4E-06	1.9E-06	1.5E-06
	85	1.2E-05	1.2E-05	1.1E-05	1.0E-05	9.1E-06	7.6E-06	5.3E-06	3.9E-06	3.2E-06	2.9E-06
	90	1.5E-05	1.4E-05	1.4E-05	1.3E-05	1.2E-05	1.0E-05	7.3E-06	5.6E-06	4.9E-06	4.4E-06
Bradenton	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	9.8E-07	7.0E-07	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	5.8E-06	5.1E-06	4.4E-06	3.2E-06	2.2E-06	1.2E-06	2.1E-07	7.0E-08	7.0E-08	7.0E-08
	75	8.5E-06	7.9E-06	7.1E-06	5.9E-06	4.8E-06	3.2E-06	1.4E-06	5.6E-07	3.5E-07	2.1E-07
	80	1.1E-05	1.1E-05	9.9E-06	8.6E-06	7.6E-06	5.6E-06	3.4E-06	2.0E-06	1.5E-06	1.2E-06
	85	1.4E-05	1.3E-05	1.3E-05	1.1E-05	1.0E-05	8.3E-06	5.6E-06	3.9E-06	3.4E-06	2.9E-06
	90	1.7E-05	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.1E-05	8.1E-06	6.2E-06	5.4E-06	4.8E-06
Flint	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	0.0E+00	0.0E+00	0.0E+00
	60	1.3E-06	9.8E-07	7.0E-07	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	4.6E-06	4.4E-06	3.9E-06	3.1E-06	2.4E-06	1.4E-06	4.9E-07	7.0E-08	7.0E-08	7.0E-08
	75	6.3E-06	6.0E-06	5.6E-06	4.9E-06	4.2E-06	2.9E-06	1.5E-06	7.7E-07	5.6E-07	3.5E-07
	80	7.8E-06	7.6E-06	7.2E-06	6.5E-06	5.9E-06	4.6E-06	2.9E-06	2.0E-06	1.7E-06	1.3E-06
	85	9.4E-06	9.1E-06	8.8E-06	8.0E-06	7.4E-06	6.2E-06	4.4E-06	3.4E-06	2.9E-06	2.5E-06
	90	1.1E-05	1.1E-05	1.1E-05	1.0E-05	9.4E-06	7.9E-06	6.0E-06	4.6E-06	4.2E-06	3.9E-06
Tallahassee	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	1.1E-06	7.7E-07	4.9E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	5.1E-06	4.6E-06	3.9E-06	3.1E-06	2.2E-06	1.2E-06	2.1E-07	7.0E-08	7.0E-08	7.0E-08
	75	7.1E-06	6.6E-06	6.1E-06	5.1E-06	4.4E-06	3.1E-06	1.4E-06	5.6E-07	3.5E-07	2.1E-07
	80	9.0E-06	8.6E-06	8.0E-06	7.2E-06	6.3E-06	5.1E-06	3.1E-06	2.0E-06	1.5E-06	1.3E-06
	85	1.1E-05	1.1E-05	1.0E-05	9.3E-06	8.5E-06	7.1E-06	5.1E-06	3.7E-06	3.2E-06	2.7E-06
	90	1.3E-05	1.3E-05	1.3E-05	1.2E-05	1.1E-05	9.5E-06	7.1E-06	5.5E-06	4.9E-06	4.4E-06
Yakima	50	1.3E-06	9.8E-07	7.0E-07	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	3.9E-06	3.4E-06	2.9E-06	2.2E-06	1.5E-06	7.7E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	6.1E-06	5.8E-06	5.3E-06	4.4E-06	3.7E-06	2.7E-06	1.5E-06	7.7E-07	5.6E-07	3.5E-07
	75	7.3E-06	6.9E-06	6.5E-06	5.6E-06	4.9E-06	3.9E-06	2.4E-06	1.5E-06	1.3E-06	1.1E-06
	80	8.6E-06	8.3E-06	7.8E-06	6.9E-06	6.1E-06	5.1E-06	3.4E-06	2.5E-06	2.2E-06	1.8E-06
	85	1.0E-05	9.9E-06	9.4E-06	8.5E-06	7.7E-06	6.3E-06	4.6E-06	3.4E-06	3.1E-06	2.7E-06
	90	1.2E-05	1.2E-05	1.2E-05	1.1E-05	9.6E-06	8.1E-06	6.1E-06	4.8E-06	4.4E-06	3.9E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.

Cancer Risk Estimate = Q* (2.5 x 10-5 $\mu g/m^{3\,-1}$) x Air concentration at a given distance ($\mu g/m^3$; see Appendix E) x Amortization factors [(8 application days/365-day year) x (5 years exposed/78-yr lifetime).

Highlighted column indicates buffer zone proposed on label for this use.

Table F9. Cancer Risk Estimates for Varied Distances from a 10-Acre Treated Field - Ornamentals[1] 5-yr Exposure											
Meteorological Region	%ile	Distance									
		5 m	7 m	10 m	15 m	20 m	30 m	50 m	70 m	80 m	90 m
Ventura	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	3.4E-06	2.9E-06	2.2E-06	1.3E-06	7.0E-07	2.1E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	7.9E-06	7.4E-06	6.6E-06	5.5E-06	4.6E-06	3.1E-06	1.3E-06	4.9E-07	2.1E-07	7.0E-08
	75	9.9E-06	9.5E-06	8.8E-06	7.7E-06	6.6E-06	5.1E-06	2.9E-06	1.8E-06	1.3E-06	9.8E-07
	80	1.2E-05	1.1E-05	1.1E-05	9.7E-06	8.8E-06	7.2E-06	4.9E-06	3.4E-06	2.9E-06	2.4E-06
	85	1.4E-05	1.4E-05	1.3E-05	1.2E-05	1.1E-05	9.5E-06	7.1E-06	5.5E-06	4.9E-06	4.4E-06
	90	1.8E-05	1.8E-05	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.0E-05	8.0E-06	7.3E-06	6.7E-06
Bakersfield	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	3.2E-06	2.9E-06	2.4E-06	1.5E-06	1.1E-06	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	7.8E-06	7.4E-06	6.8E-06	6.0E-06	5.1E-06	3.9E-06	2.2E-06	1.2E-06	7.7E-07	5.6E-07
	75	1.0E-05	9.6E-06	9.0E-06	8.0E-06	7.2E-06	5.8E-06	3.7E-06	2.5E-06	2.0E-06	1.7E-06
	80	1.2E-05	1.2E-05	1.1E-05	1.0E-05	9.4E-06	7.8E-06	5.5E-06	3.9E-06	3.4E-06	2.9E-06
	85	1.5E-05	1.5E-05	1.4E-05	1.3E-05	1.2E-05	1.0E-05	7.4E-06	5.8E-06	5.1E-06	4.4E-06
	90	1.8E-05	1.8E-05	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.0E-05	7.9E-06	7.2E-06	6.5E-06
Bradenton	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	2.2E-06	1.8E-06	1.2E-06	5.6E-07	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	8.1E-06	7.6E-06	6.6E-06	5.4E-06	4.4E-06	2.7E-06	1.1E-06	3.5E-07	2.1E-07	7.0E-08
	75	1.1E-05	1.1E-05	9.6E-06	8.3E-06	7.2E-06	5.4E-06	3.1E-06	1.7E-06	1.3E-06	9.8E-07
	80	1.4E-05	1.4E-05	1.3E-05	1.1E-05	1.0E-05	8.3E-06	5.5E-06	3.9E-06	3.2E-06	2.7E-06
	85	1.7E-05	1.7E-05	1.6E-05	1.5E-05	1.3E-05	1.1E-05	8.1E-06	6.1E-06	5.4E-06	4.8E-06
	90	2.1E-05	2.1E-05	2.0E-05	1.8E-05	1.7E-05	1.5E-05	1.1E-05	8.8E-06	7.9E-06	7.2E-06
Flint	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	0.0E+00
	60	2.5E-06	2.2E-06	1.7E-06	1.1E-06	5.6E-07	2.1E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	6.5E-06	6.1E-06	5.6E-06	4.8E-06	4.1E-06	2.9E-06	1.4E-06	5.6E-07	3.5E-07	2.1E-07
	75	8.3E-06	7.9E-06	7.4E-06	6.7E-06	6.0E-06	4.6E-06	2.9E-06	1.9E-06	1.5E-06	1.2E-06
	80	9.9E-06	9.6E-06	9.3E-06	8.5E-06	7.8E-06	6.5E-06	4.6E-06	3.4E-06	2.9E-06	2.5E-06
	85	1.2E-05	1.2E-05	1.1E-05	1.0E-05	9.6E-06	8.3E-06	6.3E-06	5.1E-06	4.4E-06	3.9E-06
	90	1.4E-05	1.4E-05	1.4E-05	1.3E-05	1.2E-05	1.0E-05	8.1E-06	6.6E-06	6.0E-06	5.5E-06
Tallahassee	50	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	2.4E-06	1.9E-06	1.3E-06	7.0E-07	3.5E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	70	7.1E-06	6.6E-06	6.0E-06	4.9E-06	4.1E-06	2.7E-06	1.1E-06	3.5E-07	2.1E-07	7.0E-08
	75	9.3E-06	8.9E-06	8.3E-06	7.3E-06	6.3E-06	4.9E-06	2.9E-06	1.8E-06	1.3E-06	9.8E-07
	80	1.1E-05	1.1E-05	1.1E-05	9.6E-06	8.6E-06	7.2E-06	5.1E-06	3.6E-06	3.1E-06	2.7E-06
	85	1.4E-05	1.4E-05	1.3E-05	1.2E-05	1.1E-05	9.6E-06	7.2E-06	5.6E-06	5.1E-06	4.6E-06
	90	1.7E-05	1.6E-05	1.6E-05	1.5E-05	1.4E-05	1.2E-05	9.9E-06	7.9E-06	7.2E-06	6.7E-06
Yakima	50	2.4E-06	2.0E-06	1.5E-06	9.8E-07	4.9E-07	7.0E-08	7.0E-08	7.0E-08	7.0E-08	7.0E-08
	60	5.1E-06	4.8E-06	4.2E-06	3.4E-06	2.7E-06	1.8E-06	7.0E-07	2.1E-07	7.0E-08	7.0E-08
	70	7.8E-06	7.4E-06	6.8E-06	6.0E-06	5.3E-06	4.1E-06	2.7E-06	1.7E-06	1.4E-06	1.1E-06
	75	9.3E-06	8.9E-06	8.4E-06	7.4E-06	6.6E-06	5.4E-06	3.7E-06	2.7E-06	2.2E-06	2.0E-06
	80	1.1E-05	1.0E-05	9.9E-06	9.0E-06	8.1E-06	6.8E-06	5.1E-06	3.9E-06	3.4E-06	2.9E-06
	85	1.3E-05	1.2E-05	1.2E-05	1.1E-05	1.0E-05	8.5E-06	6.5E-06	5.1E-06	4.6E-06	4.2E-06
	90	1.5E-05	1.5E-05	1.5E-05	1.3E-05	1.2E-05	1.1E-05	8.4E-06	6.8E-06	6.2E-06	5.6E-06

[1] Based on 6-hour average whole field PERFUM run estimated from the Ft. Pierce, Florida (turf) Field 3 flux profile, with an application rate of 69.5 lb ai/A, adjusted to reflect the 47.7 lb ai/A rate for ornamentals.
Cancer Risk Estimate = Q* (2.5 x 10-5 $\mu g/m^{3\,-1}$) x Air concentration at a given distance ($\mu g/m^3$; see Appendix E) x Amortization factors [(8 application days/365-day year) x (5 years exposed/78-yr lifetime).
Highlighted column indicates buffer zone proposed on label for this use.

APPENDIX G: 10- and 5-Year Amortized Cancer Risk Estimates for Occupational Handlers

Table G1. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 10-Year Exposure – Private Owner/Grower

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Mixer/Loader								
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves) 29.1 (gloves + DL) 8.6 (closed system)	Bare Soil	69.5	40	10	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**2E-5** **3E-5 (gloves)** **3E-5 (gloves + DL)** **2E-5 (G/DL + resp)** **8E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Bare Soil	69.5	40	10	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**2E-5** **3E-5 (gloves)** **3E-5 (gloves + DL)** **2E-5 (G/DL + resp)** **8E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Ornamentals	47.7	10	10	0.00046 0.000079 (gloves) 0.000061 (gloves + DL) 0.000018 (closed system)	**6E-5** **1E-5 (gloves)** **9E-6 (gloves + DL)** **8E-6 (G/DL + resp)** **3E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000046 0.00000046 (resp) 0.0000017 (closed system)	
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	10	0.00067 0.00012 (gloves) 0.0000889 (gloves + DL) 0.000026 (closed system)	**9E-5** **2E-5 (gloves)** **1E-5 (gloves + DL)** **1E-5 (G/DL + resp)** **4E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000067 0.00000067 (resp) 0.0000025 (closed system)	
Applicator								

Table G1. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 10-Year Exposure – Private Owner/Grower

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6 16.1 (gloves) 12.6 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	10	0.00024 0.000049 (gloves) 0.000039 (gloves + DL)	**3E-5** **8E-6 (gloves)** **6E-6 (gloves + DL)** **5E-6 (G/DL + resp)**
	Inhalation	0.34 0.034 (resp)					0.0000104 0.00000104 (resp)	
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	10	0.000031	**4E-6**
	Inhalation	0.043 (closed cab)					0.0000026	
Mixer/Loader/Applicator								
(8) Mixing/Loading Liquid and Applying with Mechanically-pressurized Handgun Sprayer	Dermal	6,050 2,050 (gloves) 1,360 (gloves+DL)	Ornamentals (soil drench)	0.0034 (lb ai/gal)	1,000 (gal/day)	10	0.000091 0.000031 (gloves) 0.000020 (gloves + DL)	**1E-5** **4E-6 (gloves)** **3E-6 (gloves + DL)** **3E-6 (G/DL + resp)**
	Inhalation	8.68 0.87 (resp)					0.0000013 0.00000013 (resp)	

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Days Exposed/Treatments per year is based on a standard assumption for a private owner/grower. Note, the assumption of 10 days per year does not account for commercial applicators completing multiple applications for multiple clients; for estimates regarding commercial applicators (30 days exposure) – See Table G2.

[5] LADD (mg/kg/day) = Daily Dose (mg/kg/day) × [Days exposed/treatments per year (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (10 yrs for existing uses; 5 yrs for proposed bare soil use) ÷ Lifetime expectancy (yrs)]; where Daily Dose = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated * Absorption factor (10% for dermal; 100% for inhalation) / Body Weight (80 kg)

[6] Cancer risk estimates = Total LADD [Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day)] × Q_1^*, where Q_1^* = **0.131** (mg/kg/day)$^{-1}$

Table G2. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 10-Year Exposure – Commercial Operations

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Mixer/Loader								
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves) 29.1 (gloves + DL) 8.6 (closed system)	Bare Soil	69.5	40	30	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**6E-5** **9E-5 (gloves)** **9E-5 (gloves + DL)** **6E-5 (G/DL + resp)** **2E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Bare Soil	69.5	40	30	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**6E-5** **9E-5 (gloves)** **9E-5 (gloves + DL)** **6E-5 (G/DL + resp)** **2E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Ornamentals	47.7	10	30	0.00046 0.000079 (gloves) 0.000061 (gloves + DL) 0.000018 (closed system)	**2E-4** **3E-5 (gloves)** **3E-5 (gloves + DL)** **2E-5 (G/DL + resp)** **9E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000046 0.00000046 (resp) 0.0000017 (closed system)	
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	30	0.00067 0.00012 (gloves) 0.0000889 (gloves + DL) 0.000026 (closed system)	**3E-4** **6E-5 (gloves)** **3E-5 (gloves + DL)** **3E-5 (G/DL + resp)** **1E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000067 0.00000067 (resp) 0.0000025 (closed system)	
Applicator								
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6 16.1 (gloves) 12.6 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	30	0.00024 0.000049 (gloves) 0.000039 (gloves + DL)	**9E-5** **2E-5 (gloves)** **2E-5 (gloves + DL)**

Table G2. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 10-Year Exposure – Commercial Operations

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
	Inhalation	0.34 0.034 (resp)					0.0000104 0.00000104 (resp)	**1E-5 (G/DL + resp)**
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	30	0.000031	**1E-5**
	Inhalation	0.043 (closed cab)					0.0000026	
Mixer/Loader/Applicator								
(8) Mixing/Loading Liquid and Applying with Mechanically-pressurized Handgun Sprayer	Dermal	6,050 2,050 (gloves) 1,360 (gloves+DL)	Ornamentals (soil drench)	0.0034 (lb ai/gal)	1,000 (gal/day)	30	0.000091 0.000031 (gloves) 0.000020 (gloves + DL)	**3E-5** **1E-5 (gloves)** **9E-6 (gloves + DL)**
	Inhalation	8.68 0.87 (resp)					0.0000013 0.00000013 (resp)	**9E-6 (G/DL + resp)**

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Days Exposed/Treatments per year is based on a standard assumption for commercial applicators completing multiple applications for multiple clients; 30 days.

[5] LADD (mg/kg/day) = Daily Dose (mg/kg/day) × [Days exposed/treatments per year (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (10 yrs for existing uses; 5 yrs for proposed bare soil use) ÷ Lifetime expectancy (yrs)]; where Daily Dose = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated * Absorption factor (10% for dermal; 100% for inhalation) / Body Weight (80 kg)

[6] Cancer risk estimates = Total LADD [Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day)] × Q_1^*, where Q_1^* = **0.131** $(mg/kg/day)^{-1}$

Table G3. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 5-Year Exposure – Private Owner/Grower

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Mixer/Loader								
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves) 29.1 (gloves + DL) 8.6 (closed system)	Bare Soil	69.5	40	10	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**2E-5** **3E-5 (gloves)** **3E-5 (gloves + DL)** **2E-5 (G/DL + resp)** **8E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Bare Soil	69.5	40	10	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**2E-5** **3E-5 (gloves)** **3E-5 (gloves + DL)** **2E-5 (G/DL + resp)** **8E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Ornamentals	47.7	10	10	0.00023 0.000039 (gloves) 0.000031 (gloves + DL) 0.0000090 (closed system)	**3E-5** **5E-6 (gloves)** **4E-6 (gloves + DL)** **4E-6 (G/DL + resp)** **1E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000023 0.00000023 (resp) 0.00000087 (closed system)	
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	10	0.00034 0.000057 (gloves) 0.000044 (gloves + DL) 0.000013 (closed system)	**4E-5** **8E-6 (gloves)** **6E-6 (gloves + DL)** **6E-6 (G/DL + resp)** **2E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000033 0.0000033 (resp) 0.0000013 (closed system)	
Applicator								

Table G3. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 5-Year Exposure – Private Owner/Grower

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6 16.1 (gloves) 12.6 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	**10**	10	0.00012 0.000025 (gloves) 0.000019 (gloves + DL)	**2E-5** **4E-6 (gloves)** **3E-6 (gloves + DL)** **3E-6 (G/DL + resp)**
	Inhalation	0.34 0.034 (resp)					0.0000052 0.00000052 (resp)	
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	10	0.000031	**4E-6**
	Inhalation	0.043 (closed cab)					0.0000026	
Mixer/Loader/Applicator								
(8) Mixing/Loading Liquid and Applying with Mechanically-pressurized Handgun Sprayer	Dermal	6,050 2,050 (gloves) 1,360 (gloves+DL)	Ornamentals (soil drench)	0.0034 (lb ai/gal)	1,000 (gal/day)	10	0.000045 0.000015 (gloves) 0.0000102 (gloves + DL)	**6E-6** **2E-6 (gloves)** **1E-6 (gloves + DL)** **1E-6 (G/DL + resp)**
	Inhalation	8.68 0.87 (resp)					0.00000065 0.000000065 (resp)	

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Days Exposed/Treatments per year is based on a standard assumption for a private owner/grower. Note, the assumption of 10 days per year does not account for commercial applicators completing multiple applications for multiple clients; for estimates regarding commercial applicators (30 days exposure) – See Table G4.

[5] LADD (mg/kg/day) = Daily Dose (mg/kg/day) × [Days exposed/treatments per year (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (5 yrs) ÷ Lifetime expectancy (yrs)]; where Daily Dose = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated * Absorption factor (10% for dermal; 100% for inhalation) / Body Weight (80 kg)

[6] Cancer risk estimates = Total LADD [Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day)] × Q_1^*, where Q_1^* = **0.131** $(mg/kg/day)^{-1}$

Table G4. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 5-Year Exposure – Commercial Operations

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
Mixer/Loader								
(1) Mixing/Loading Liquid for Shank Injection	Dermal	220 37.6 (gloves) 29.1 (gloves + DL) 8.6 (closed system)	Bare Soil	69.5	40	30	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**6E-5** **9E-5 (gloves)** **9E-5 (gloves + DL)** **6E-5 (G/DL + resp)** **2E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
(2) Mixing/Loading Liquid for Chemigation	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Bare Soil	69.5	40	30	0.0013 0.00023 (gloves) 0.00018 (gloves + DL) 0.000053 (closed system)	**6E-5** **9E-5 (gloves)** **9E-5 (gloves + DL)** **6E-5 (G/DL + resp)** **2E-5 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.000013 0.0000013 (resp) 0.0000051 (closed system)	
	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Ornamentals	47.7	10	30	0.00023 0.000039 (gloves) 0.000031 (gloves + DL) 0.0000090 (closed system)	**9E-5** **2E-5 (gloves)** **1E-5 (gloves + DL)** **1E-5 (G/DL + resp)** **3E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000023 0.00000023 (resp) 0.00000087 (closed system)	
(3) Mixing/Loading Liquid for Groundboom application	Dermal	220 37.6 (gloves) 29.1 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	30	0.00034 0.000057 (gloves) 0.000044 (gloves + DL) 0.000013 (closed system)	**1E-4** **2E-5 (gloves)** **2E-5 (gloves + DL)** **2E-5 (G/DL + resp)** **6E-6 (closed system)**
	Inhalation	0.219 0.0219 (resp)					0.0000033 0.0000033 (resp) 0.0000013 (closed system)	
Applicator								
(4) Applying Sprays with Open Cab Groundboom	Dermal	78.6 16.1 (gloves) 12.6 (gloves + DL)	Golf course, Athletic Fields & Sod Farms	69.5	10	30	0.00012 0.000025 (gloves) 0.000019 (gloves + DL)	**6E-5** **1E-5 (gloves)** **9E-6 (gloves + DL)**

Table G4. Summary of Cancer Risk Estimates for Occupational Handlers of Furfural – 5-Year Exposure – Commercial Operations

Exposure Scenario (Scenario #)	Exposure Route	Unit Exposure (µg/lb ai) [1]	Use Site	Application Rate (lb ai/A)[2]	Area Treated (A/day) [3]	Days Exposed/ Treatments (days/yr) [4]	LADD (mg/kg/day) [5]	Total Cancer Risk [6]
	Inhalation	0.34 0.034 (resp)					0.0000052 0.00000052 (resp)	**9E-6 (G/DL + resp)**
(5) Applying via Shank Injection (Closed Cab Groundboom used as surrogate)	Dermal	5.1 (closed cab)	Bare Soil	69.5	40	30	0.000031	**1E-5**
	Inhalation	0.043 (closed cab)					0.0000026	
Mixer/Loader/Applicator								
(8) Mixing/Loading Liquid and Applying with Mechanically-pressurized Handgun Sprayer	Dermal	6,050 2,050 (gloves) 1,360 (gloves+DL)	Ornamentals (soil drench)	0.0034 (lb ai/gal)	1,000 (gal/day)	30	0.000045 0.000015 (gloves) 0.0000102 (gloves + DL)	**2E-5** **6E-6 (gloves)** **3E-6 (gloves + DL)** **3E-6 (G/DL + resp)**
	Inhalation	8.68 0.87 (resp)					0.00000065 0.000000065 (resp)	

[1] Baseline dermal unit exposure values represent long pants, long sleeved shirts, shoes, and socks; PPE values represent the addition of chemical-resistant gloves, gloves plus double layer of clothing (i.e., coveralls over baseline clothing), or engineering controls (i.e., closed system) for those scenarios in which the MOEs do not reach 100 at baseline or with gloves and coveralls. Baseline inhalation unit exposure values represent no respiratory protection, while PPE values represent the addition of a respirator providing 90% reduction of baseline inhalation exposure. Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (September 26, 2011); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline and PPE (gloves, double layer of clothing and respirator)).

[2] Application rates are based on maximum values found in label: MULTIGUARD PROTECT® EC (EPA Reg No: 75753-1).

[3] Daily area treated is based on the proposed label which limits the number of acres that may be treated in a 24-hour period to 10 for ornamentals, athletic fields and sod farms and 40 for bare soil farms. For the other scenarios it is based on standard EPA/OPP/HED values for the area or gallons that can be reasonably applied in a single day for the application method and formulation/packaging type.

[4] Days Exposed/Treatments per year is based on a standard assumption for commercial applicators completing multiple applications for multiple clients; 30 days.

[5] LADD (mg/kg/day) = Daily Dose (mg/kg/day) × [Days exposed/treatments per year (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (5 yrs) ÷ Lifetime expectancy (yrs)]; where Daily Dose = (Unit Exposure [dermal or inhalation] * cf [0.001mg/µg] * Application rate * Area treated * Absorption factor (10% for dermal; 100% for inhalation) / Body Weight (80 kg)

[6] Cancer risk estimates = Total LADD [Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day)] × Q_1^*, where Q_1^* = **0.131** (mg/kg/day)$^{-1}$